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(71) Applicant: **GENENEWS CORPORATION 2 EAST BEAVER CREEK ROAD, BUILDING 2, RICHMOND HILL, ONTARIO L4B 2N3 CA**

(72) Inventor: **LIEW, CHOONG-CHIN 81 MILLERSGROVE DRIVE, TORONTO, ONTARIO , M2R 3S1 CA**
CHAO, SAMUEL 114 GLEN SHIELDS AVENUE, CONCORD, ONTARIO , L4K 1T6 CA

(54) **Title:**
METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT

(57) **Abstract:**
METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT Abstract A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer is disclosed. The method comprises, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 : determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Fig 1A

METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT

Abstract

A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer is disclosed. The method comprises, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 : determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

Fig 1A

METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of US provisional application 61/123,798, filed April 10, 2008 and of US provisional application 61/123,831, filed April 11, 2008. The entire contents of both provisional applications are incorporated by reference herein.

TECHNICAL FIELD

The disclosure relates to apparatuses, kits and methods for determining a probability of colorectal cancer in a test subject. More particularly, the disclosure relates to apparatuses, kits and methods for diagnosing colorectal cancer in a test subject by measuring a level of one or more gene products in blood of the test subject.

BACKGROUND

Colorectal cancer causes 655,000 deaths worldwide per year, making it the second-leading cause of cancer-related deaths. It is the third most frequently diagnosed cancer in men and women in the United States and carries an overall population lifetime risk of 6%. (American Cancer Society. Cancer Facts and Figures. 2008. Atlanta: American Cancer Society.). The American Cancer Society estimates that about 108,070 new cases of colon cancer (53,760 in men and 54,310 in women) and 40,740 new cases of rectal cancer (23,490 in men and 17,250 in women) will be diagnosed in 2008. Of those diagnosed, nearly half are expected to die within five years. In the United States in 2008 an estimated 50,000 men and women will die of cancer of the colon and rectum. (American Cancer Society 2008). This high mortality rate is due at least in part to the fact that a large proportion of cancers are detected at relatively late stages, such as following onset of overt symptoms, when the cancer is more difficult to treat. In addition, identification of colorectal cancer at later stages concomitantly necessitates harsher treatment, such as radical colostomy. It has been shown that the identification and treatment of colorectal cancer at earlier stages significantly reduces the risk of developing more advanced disease, and hence risk of death from the disease. Stage at detection is critically related to patient survival. Localized cancers (Dukes's Stage A or B) have an excellent prognosis of 82% - 93% at five years. Regional (Dukes's Stage C) patients have a five year survival rates of 55% to 60%; and only 5% to 8% of patients with late stage cancer will survive the five year span. (O'Connell JB, Maggard M, Ko CY. Colon cancer survival rates with the new American Joint Committee on cancer sixth edition staging. JNCI. 2004; 96: 1420-1425.). Therefore, a test to screen for colorectal cancer so as to allow earlier treatment should markedly reduce the incidence of advanced-stage colorectal cancer (Ransohoff DF. Colorectal cancer screening in 2005: status and challenges. Gastroenterology. 2005 May;128(6):1685-95) and decrease the current costs to the medical system. Thus, the American Cancer Society recommends that all Americans age 50 and older be screened regularly for colorectal cancer. Unfortunately, only a small fraction of the population at risk is screened for the disease (Mitka M. Colorectal cancer screening rates still fall far short of recommended levels. JAMA. 2008 Feb 13;299(6):622), as currently available screening methods require insufficiently available and/or costly resources, are associated with unacceptably low patient compliance, and/or are associated with significant health risks.

Currently utilized screening technologies to test for colorectal cancer include fecal occult blood test (FOBT), flexible sigmoidoscopy, double contrast barium enema (DCBE), and colonoscopy. The current recommended standards for screening for colorectal cancer in individuals over the age of 50 and who are considered part of an average risk population include: an FOBT yearly, a sigmoidoscopy every five years, a colonoscopy every ten years and a DCBE every five years. For a high risk population where one or more family members have had colorectal cancer, a colonoscopy is recommended every two years as a follow up to FOBT or sigmoidoscopy. Each of these tests suffers significant disadvantages. Fecal occult blood testing suffers from low sensitivity, requires significant dietary and other restrictions prior to testing and is associated with poor patient compliance. Sigmoidoscopy and colonoscopy are more sensitive than the other standard methods since they involve direct visualization of the lumen of the colon, however these methods are also associated with various significant disadvantages. Sigmoidoscopy and colonoscopy are both highly invasive procedures which cause significant levels of discomfort, causing many individuals to opt not to undergo these recommended screening procedures. Sigmoidoscopy only allows visualization of the distal part of the colon and hence cannot detect a relatively large fraction of cancers, and colonoscopy, despite allowing examination essentially along the entire length of the colon, is associated with a significant failure rate for detection of colorectal cancer. In addition, sigmoidoscopy and colonoscopy are costly, are insufficiently available, and may result in potentially lethal complications, such as accidental intestinal perforation.

Various approaches have been proposed in the prior art for colorectal cancer testing using identification and analysis of markers of this disease in blood (reviewed in Hundt S. *et al.* Blood markers for early detection of colorectal cancer: a systematic review. Cancer Epidemiol Biomarkers Prev. 2007 Oct;16(10):1935-53). Such approaches, if successful, would have the advantage of circumventing critical disadvantages of the standard prior art methods, by virtue, for example, of being relatively non-invasive, minimally cumbersome, essentially risk-free and hence likely to be associated with increased patient screening compliance rates. However, none of these approaches has demonstrated an optimal capacity for diagnosing colorectal cancer. Thus, there is a longstanding and urgent need for an improved method of determining a probability of colorectal cancer in a subject based on analysis of blood markers.

SUMMARY

The invention discloses novel methods, apparatuses and kits for determining a probability of colorectal cancer in a subject, based on novel blood markers of colorectal cancer. This use can be effected in a variety of ways as further described and exemplified herein.

According to one aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data; (b) providing positive

control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to yet another aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to one aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to still another aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data; (b) providing positive

control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to a further aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to yet a further aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to still a further aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data; (b) providing positive

control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to further features of the invention described below, the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject.

According to further features of the invention described below, the method of determining the probability that the human test subject has colorectal cancer as opposed to not having colorectal cancer further comprises determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer.

According to further features of the invention described below, the determining of the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data, wherein the mathematical model is for determining the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the invention there is provided a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to another aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to another aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet another aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to still another aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to a further aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet a further aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to still a further aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to an additional aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet an additional aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a CLEC4D gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to still an additional aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a IL2RB gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet still an additional aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a LMNB1 gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to another aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a PRRG4 gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet another aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to still another aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a VNN1 gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to a further aspect of the present invention there is provided a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control dataa mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and wherein, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to yet a further aspect of the present invention there is provided a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, computer-implemented steps of: applying to test data representing a level of RNA encoded by the gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a formula for calculating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and wherein, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to one aspect of the invention there is provided a method of diagnosing colorectal cancer in a test subject, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, wherein a determination that the test data corresponds to the positive control data and not to the negative control data provides an indication of colorectal cancer in the test subject.

According to a further aspect of the present invention there is provided a method of diagnosing colorectal cancer in a test subject, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer provides an indication of colorectal cancer in the test subject, and wherein, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer provides an indication of colorectal cancer in the test subject.

According to another aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a annexin A3 (ANXA3) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to yet another aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a C-type lectin domain family 4, member D (CLEC4D) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to still another aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a interleukin 2 receptor, beta (IL2RB) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood.

According to a further aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a lamin B1 (LMNB1) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to yet a further aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a proline rich Gla (G carboxyglutamic acid) 4 (transmembrane) (PRRG4) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to still a further aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a tumor necrosis factor, alpha induced protein 6 (TNFAIP6) gene in the test sample of blood, ii) comparing the level of RNA encoded by as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to still a further aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and i) determining a level of RNA encoded by a vanin 1 (VNN1) gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

According to an additional aspect of the present invention there is provided a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: a) obtaining a test sample of blood from the subject; and for each gene of a set of genes selected from the group consisting of : ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, i) determining a level of RNA encoded by the gene in the test sample of blood, ii) comparing the level of RNA encoded by the gene of the set as determined in step (i) with the level of RNA encoded by the gene in one or more control samples of blood; and b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for IL2RB, the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood.

According to an additional aspect of the present invention there is provided a method of diagnosing colorectal cancer in a test subject, comprising: a) obtaining a test sample of blood from the subject; and for each gene of a set of genes selected from the group consisting of : ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, i) determining a level of RNA encoded by the gene in the test sample of blood, and ii) applying to the level of RNA encoded by the gene of the set as determined in step (i) and to the level of RNA encoded by the gene in one or more control samples of blood a mathematical formula for generating a value indicating whether, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and, for IL2RB, the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood; and b) concluding that there is an indication of colorectal cancer in the test subject, if, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the value indicates that the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and concluding that there is an indication of colorectal cancer in the test subject if, for IL2RB, the value indicates that the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood.

According to further features of the invention described below, the control samples are from individuals who have been diagnosed as not having colorectal cancer.

According to still another aspect of the invention there is provided a kit comprising packaging and containing, for each gene of a set of two or more genes selected from the group consisting of ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, a primer set capable of generating an amplification product of a polynucleotide complementary to RNA encoded, in a human subject, only by the gene.

According to further features of the invention described below, the kit further contains two or more components selected from the group consisting of a thermostable polymerase, a reverse transcriptase, deoxynucleotide triphosphates, nucleotide triphosphates and enzyme buffer.

According to further features of the invention described below, the kit further contains at least one labeled probe capable of selectively hybridizing to either a sense or an antisense strand of the amplification product.

According to further features of the invention described below, the kit further contains a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying a mathematical model to test data representing a level of RNA encoded by the gene in blood of a human test subject, wherein the mathematical model is derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, and wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

According to further features of the invention described below, the kit further contains a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying, to test data representing a level of RNA encoded by the gene in blood of a human test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and wherein, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

According to further features of the invention described below, the set of one or more genes consists of ACTB and one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1.

According to further features of the invention described below, the set of one or more genes consists of ACTB and ANXA3.

According to further features of the invention described below, the set of one or more genes consists of ACTB and CLEC4D.

According to further features of the invention described below, the set of one or more genes consists of ACTB and IL2RB.

According to further features of the invention described below, the set of one or more genes consists of ACTB and LMNB1.

According to further features of the invention described below, the set of one or more genes consists of ACTB and PRRG4.

According to further features of the invention described below, the set of one or more genes consists of TNFAIP6 and PRRG4.

According to further features of the invention described below, the set of one or more genes consists of ACTB and VNN1.

According to further features of the invention described below, the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

According to further features of the invention described below, the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

According to further features of the invention described below, the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

According to further features of the invention described below, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1.

According to further features of the invention described below, the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

According to further features of the invention described below, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

According to further features of the invention described below, the set of one or more genes consists of ANXA3.

According to further features of the invention described below, the set of one or more genes consists of CLEC4D.

According to further features of the invention described below, the set of one or more genes consists of IL2RB.

According to further features of the invention described below, the set of one or more genes consists of LMNB1.

According to further features of the invention described below, the set of one or more genes consists of PRRG4.

According to further features of the invention described below, the set of one or more genes consists of TNFAIP6.

According to further features of the invention described below, the set of one or more genes consists of VNN1.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and ANXA3.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and CLEC4D.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and LMNB1.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and PRRG4.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and TNFAIP6.

According to further features of the invention described below, the set of one or more genes consists of IL2RB and VNN1.

Definitions:

As will become apparent, preferred features and characteristics of one aspect of the invention are applicable to any other aspect of the invention. It should be noted that, as used herein, the singular form "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

"Encode" A polynucleotide, including a gene, is said the to "encode" a RNA and/or polypeptide if, in its native state or when manipulated by methods well known to those skilled in the art, it can be transcribed and/or translated to produce the mRNA for and/or the polypeptide or a fragment thereof. The anti-sense strand is the complement of such a nucleic acid, and the encoding sequence can be deduced there from.

The term "label" refers to a composition capable of producing a detectable signal indicative of the presence of the target polynucleotide in an assay sample. Suitable labels include radioisotopes, nucleotide chromophores, enzymes, substrates, fluorescent molecules, chemiluminescent moieties, magnetic particles, bioluminescent moieties, and the like. As such, a label is any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical means.

As used herein, a "sample" refers to a sample of tissue or fluid isolated from an individual, including but not limited to, for example, blood, plasma, serum, tumor biopsy, urine, stool, sputum, spinal fluid, pleural fluid, nipple aspirates, lymph fluid, the external sections of the skin, respiratory, intestinal, and genitourinary tracts, tears, saliva, milk, cells (including but not limited to blood cells), organs, and also samples of in vitro cell culture constituent.

Examples of amplification techniques include strand displacement amplification, as disclosed in U.S. Pat. No. 5,744,311; transcription-free isothermal amplification, as disclosed in U.S. Pat. No. 6,033,881; repair chain reaction amplification, as disclosed in WO 90/01069; ligase chain reaction amplification, as disclosed in European Patent Appl. 320 308; gap filling ligase chain reaction amplification, as disclosed in U.S. Pat. No. 5,427,930; and RNA transcription-free amplification, as disclosed in U.S. Pat. No. 6,025,134.

Examples of a primer of the invention include an oligonucleotide which is capable of acting as a point of initiation of polynucleotide synthesis along a complementary strand when placed under conditions in which synthesis of a primer extension product which is complementary to a polynucleotide is catalyzed. Such conditions include the presence of four different nucleotide triphosphates or nucleoside analogs and one or more agents for polymerization such as DNA polymerase and/or reverse transcriptase, in an appropriate buffer ("buffer" includes substituents which are cofactors, or which affect pH, ionic strength, etc.), and at a suitable temperature. A primer must be sufficiently long to prime the synthesis of extension products in the presence of an agent for polymerase. A typical primer contains at least about 5 nucleotides in length of a sequence substantially complementary to the target sequence, but somewhat longer primers are preferred.

The terms "complementary" or "complement thereof", as used herein, refer to sequences of polynucleotides which are capable of forming Watson & Crick base pairing with another specified polynucleotide throughout the entirety of the complementary region.

This term is applied to pairs of polynucleotides based solely upon their sequences and does not refer to any specific conditions under which the two polynucleotides would actually bind.

A primer will always contain a sequence substantially complementary to the target sequence, that is the specific sequence to be amplified, to which it can anneal.

In the context of this invention, the term "probe" refers to a molecule which can detectably distinguish between target molecules differing in structure, such as allelic variants. Detection can be accomplished in a variety of different ways but preferably is based on detection of specific binding. Examples of such specific binding include antibody binding and nucleic acid probe hybridization.

The term " gene" as used herein is a polynucleotide which may include coding sequences, intervening sequences and regulatory elements controlling transcription and/or translation. Genes of the invention include normal alleles of the gene encoding polymorphisms, including silent alleles having no effect on the amino acid sequence of the gene's encoded polypeptide as well as alleles leading to amino acid sequence variants of the encoded polypeptide that do not substantially affect its function. These terms also may otpyiosnlly include alleles having one or more mutations which affect the function of the encoded polypeptide's function.

The polynucleotide compositions, such as primers of the invention, of this invention include RNA, cDNA, DNA complementary to target cDNA of this invention or portion thereof, genomic DNA, unspliced RNA, spliced RNA, alternately spliced RNA, synthetic forms, and mixed polymers, both sense and antisense strands, and may be chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art.

Where nucleic acid according to the invention includes RNA, reference to the sequence shown should be construed as reference to the RNA equivalent, with U substituted for T.

The term "amount" or "level" of RNA encoded by a gene of the invention, preferably a colorectal cancer biomarker gene described herein, or a housekeeping gene, encompasses the absolute amount of the RNA, the relative amount or concentration of the RNA, as well as any value or parameter which correlates thereto.

The methods of nucleic acid isolation, amplification and analysis are routine for one skilled in the art and examples of protocols can be found, for example, in the Molecular Cloning: A Laboratory Manual (3-Volume Set) Ed. Joseph Sambrook, David W. Russel, and

Joe Sambrook, Cold Spring Harbor Laboratory; 3rd edition (Jan. 15, 2001), ISBN: 0879695773. Particularly useful protocol source for methods used in PCR amplification is PCR (Basics: From Background to Bench) by M. J. McPherson, S. G. Moller, R. Beynon, C. Howe, Springer Verlag; 1st edition (Oct. 15, 2000), ISBN: 0387916008.

"Kit" refers to a combination of physical elements, e.g., probes, including without limitation specific primers, labeled nucleic acid probes, antibodies, protein-capture agent(s), reagent(s), instruction sheet(s) and other elements useful to practice the invention, in particular to identify the levels of particular RNA molecules in a sample. These physical elements can be arranged in any way suitable for carrying out the invention. For example, probes and/or primers can be provided in one or more containers or in an array or microarray device.

Colorectal cancer, also called colon cancer or rectal cancer or colorectal carcinoma, is cancer that forms in either the colon or the rectum.

The present invention is useful in a diagnostic product or method to detect the level of RNA of genes of interest, in particular, the colorectal biomarkers of the present invention. Accordingly, the invention encompasses the use of diagnostic kits based on a variety of methodologies, e.g., PCR, reverse transcriptase-PCR, quantitative PCR, microarray, chip, mass-spectroscopy, which are capable of detecting RNA levels in a sample. The invention also provides an article of manufacturing comprising packaging material and an analytical agent contained within the packaging material, wherein the analytical agent can be used for determining and/or comparing the levels of RNA encoded by one or more target genes of the invention, and wherein the packaging material comprises a label or package insert which indicates that the analytical agent can be used to identify levels of RNA that correspond to a probability that a test subject has colorectal cancer, such as a probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

The present invention therefore provides kits comprising degenerate primers to amplify polymorphic alleles or variants of target genes of the invention, and instructions comprising an amplification protocol and analysis of the results. The kit may alternatively also comprise buffers, enzymes, and containers for performing the amplification and analysis of the amplification products. The kit may also be a component of a screening or prognostic kit comprising other tools such as DNA microarrays. The kit may also provides one or more control templates, such as nucleic acids isolated from sample of patientss without colorectal cancer, and/or nucleic acids isolated from ssamples of patients with colorectal cancer.

The kit may also include instructions for use of the kit to amplify specific targets on a solid support. Where the kit contains a prepared solid support having a set of primers already fixed on the solid support, e.g. for amplifying a particular set of target polynucleotides, the kit also includes reagents necessary for conducting a PCR on a solid support, for example using an in situ-type or solid phase type PCR procedure where the support is capable of PCR amplification using an in situ-type PCR machine. The PCR reagents, included in the kit, include the usual PCR buffers, a thermostable polymerase (e.g. Taq DNA polymerase), nucleotides (e.g. dNTPs), and other components and labeling molecules (e.g. for direct or indirect labeling). The kits can be assembled to support practice of the PCR amplification method using immobilized primers alone or, alternatively, together with solution phase primers.

In one embodiment, the kit provides one or more primer pairs, each pair capable of amplifying RNA encoded by a target gene of the invention, thereby providing a kit for analysis of RNA expression of several different target genes of the invention in a biological sample in one reaction or several parallel reactions. Primers in the kits may be labeled, for example fluorescently labeled, to facilitate detection of the amplification products and consequent analysis of the RNA levels.

In one embodiment, levels of RNA encoded by more than one target gene can be determined in one analysis. A combination kit may therefore include primers capable of amplifying cDNA deriived fom RNA encoded by different target genes. The primers may be differentially labeled, for example using different fluorescent labels, so as to differentiate between RNA from different target genes.

Multiplex, such as duplex, real-time RT-PCR enables simultaneous quantification of 2 targets in the same reaction, which saves time, reduces costs, and conserves samples. These advantages of multiplex, real-time RT-PCR make the technique well-suited for high-throughput gene expression analysis. Multiplex qPCR assay in a real-time format facilitates quantitative measurements and minimizes the risk of false-negative results. It is essential that multiplex PCR is optimized so that amplicons of all samples are compared insub-plateau phase of PCR. Yun, Z., I. Lewensohn-Fuchs, P. Ljungman, L. Ringholm, J. Jonsson, and J. Albert. 2003. A real-time TaqMan PCR for routine quantitation of cytomegalovirus DNA in crude leukocyte lysates from stem cell transplant patients. J. Virol. Methods 110:73-79. [PubMed]. Yun, Z., I. Lewensohn-Fuchs, P. Ljungman, and A. Vahlne. 2000. Real-time monitoring of cytomegalovirus infections after stem cell transplantation using the TaqMan polymerase chain reaction assays. Transplantation 69:1733-1736. [PubMed]. Simultaneous quantification of up to 2, 3, 4, 5, 6, 7, and 8 or more targets may be useful.

. The primers and probes contained within the kit may include those listed in 19, and various subcombinations thereof.

A "control population" refers to a defined group of individuals or a group of individuals with or without colorectal cancer, and may optionally be further identified by, but not limited to geographic, ethnic, race, gender, one or more other conditions or diseases, and/or cultural indices. In most cases a control population may encompass at least 10, 50, 100, 1000, or more individuals.

"Positive control data" encompasses data representing levels of RNA encoded by a target gene of the invention in each of one or more subjects having colorectal cancer of the invention, and encompasses a single data point representing an average level of RNA encoded by a target gene of the invention in a plurality of subjects having colorectal cancer of the invention.

"Negative control data" encompasses data representing levels of RNA encoded by a target gene of the invention in each of one or more subjects not having colorectal cancer of the invention, and encompasses a single data point representing an average level of RNA encoded by a target gene of the invention in a plurality of subjects having colorectal cancer of the invention.

The probability that test data of the invention "corresponds" to positive control data or negative control data of the invention refers to the probability that the test data is more likely to be characteristic of data obtained in subjects having colorectal cancer than in subjects not having any colorectal pathology, or is more likely to be characteristic of data obtained in subjects not having any colorectal pathology than in subjects having colorectal cancer, respectively.

A primer which "selectively hybridizes" to a target polynucleotide is a primer which is capable of hybridizing only, or mostly, with a single target polynucleotide in a mixture of polynucleotides consisting of RNA of human blood, or consisting of DNA complementary to RNA of human blood.

A gene expression profile of the invention for colorectal cancer found in blood at the RNA level of one or more genes comprising, but preferably not limited to, an ANXA3 gene, a CLEC4D gene, an IL2RB gene, an LMNB1 gene, a PRRG4 gene, a TNFAIP6 gene and a

VNN1 gene, can be identified or confirmed using many techniques, including but preferably not limited to PCR methods, as for example discussed further in the working examples herein, Nothern analyses and and the microarray technique. This gene expression profile can be measured in a bodily sample, such as blood, using microarray technology. In an embodiment of this method, fluorescently labeled cDNA probes may be generated through incorporation of fluorescent nucleotides by reverse transcription of RNA extracted from blood. Labeled cDNA probes applied to the chip hybridize with specificity to each spot of DNA on the array. Quantitation of hybridization of each arrayed element allows for assessment of corresponding mRNA abundance. For example, with dual color fluorescence, separately labeled cDNA probes generated from two sources of RNA are hybridized pair wise to the array. The relative abundance of the transcripts from the two sources corresponding to each specified gene is thus determined simultaneously. Such methods have been shown to have the sensitivity required to detect rare transcripts, which are expressed at a few copies per cell, and to reproducibly detect at least approximately two-fold differences in the expression levels (Schena et al., Proc. Natl. Acad. Sci. USA 93(2):106-149 (1996)). Microarray analysis can be performed by commercially available equipment, following manufacturer's protocols, such as by using the Affymetrix GenChip technology, or Incyte's microarray technology.

Other features and advantages of the invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples while indicating preferred embodiments of the invention are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be described in relation to the drawings in which:

FIGs 1A-H are sequence diagrams depicting the nucleotide sequences of the following genes: ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, respectively.

FIG. 2 is a schematic depicting an exemplary computer system for practicing certain of the methods described herein.

DETAILED DESCRIPTION

The invention is of methods, kits, computer systems and computer-readable media for determining a probability that a human subject has colorectal cancer. Specifically, the invention can be used to determine such a probability via analysis of novel markers of colorectal cancer in blood which are disclosed herein.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details set forth in the following description or exemplified by the Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

Effective methods of testing for colorectal cancer via analysis of blood markers would overcome critical disadvantages of prior art methods, which are excessively invasive, cumbersome, risky, unavailable and/or associated with low patient screening compliance rates. While various approaches have been proposed in the prior art for colorectal cancer testing via analysis of markers of this disease in blood (reviewed in Hundt S. *et al.* Blood markers for early detection of colorectal cancer: a systematic review. Cancer Epidemiol Biomarkers Prev. 2007 Oct;16(10):1935-53), none of these approaches, however, has demonstrated a capacity to satisfactorily enable determination of the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer.

Thus, the prior art fails to provide an effective method of testing a subject for colorectal cancer via analysis in a blood sample of levels of RNA encoded by one or more of the genes ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 blood markers.

While reducing the invention to practice it was surprisingly uncovered that levels of RNA encoded by the genes ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 are significantly higher in blood of subjects having colorectal cancer than in blood of subjects not having any colorectal pathology, and that levels of RNA encoded by IL2RB are significantly lower in blood of subjects having colorectal cancer than in blood of subjects not having any colorectal pathology (Example 2). While further reducing the invention to practice, it was surprisingly uncovered that mathematical models based on levels of RNA encoded by the 127 possible combinations of the colorectal cancer marker genes ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of a test subject could be derived capable of discriminating between subjects having colorectal cancer and subjects not having any colorectal pathology (Example 2). While further reducing the invention to practice, it was surprisingly uncovered that mathematical models based on levels of RNA encoded by the 63 possible combinations of the colorectal cancer marker genes ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6, and VNN1 in blood of a test subject, when normalized against levels of RNA encoded by IL2RB, could be derived capable of discriminating between subjects having colorectal cancer and subjects not having any colorectal pathology (Example 3). It will be appreciated that application of such mathematical models to test data representing blood levels in a test subject of RNA encoded by the aforementioned novel colorectal cancer marker genes disclosed herein can be used to provide the probability that the test subject has colorectal cancer as opposed to not having any colorectal pathology.

While reducing the invention to practice, fold changes of blood levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, including fold-changes of levels normalized to IL2RB, in subjects having colorectal cancer relative to subjects not having any colorectal pathology were surprisingly uncovered (Example 2, Example 3 and Example 6).

Thus, according to one aspect of the invention there is provided a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer. In a first step, the method is effected by determining, for each gene of a set of one or more of the colorectal cancer marker genes: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1; a level of RNA encoded by the gene in blood of the test subject, thereby generating test data. In a second step, the method is effected by determining the probability that the test data corresponds to positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer and not to negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. The probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

Thus, according to an aspect of the invention, there is provided a method of classifying a test subject as being more likely to have colorectal cancer than to not have colorectal cancer. The method of classifying is effected by determining a level of RNA encoded by one or more of the set of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and/or VNN1 in blood of the test subject, to thereby generate test data and applying to the test data, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. For ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer; and where, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

Determining whether the level of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 or VNN1 in blood of the test subject is higher than the level of RNA encoded by the gene in blood of control subjects not having colorectal cancer may be effected by determining whether there is a fold-change in the level between the test subject and the control subjects not having colorectal cancer which is higher than a minimum fold-change and/or which is within a range of fold-changes.

Determining whether the level of RNA encoded by IL2RB in blood of the test subject is lower than the level of RNA encoded by the gene in blood of control subjects not having colorectal cancer may be effected by determining whether there is a fold-change in the level between the test subject and the control subjects not having colorectal cancer which is lower than a maximum fold-change and/or which is within a range of fold-changes.

Examples of suitable fold-changes and ranges of fold-changes for classifying a test subject according to the invention are provided in Example 2, Example 3 and Example 6, below, and include the following ones.

For levels of RNA encoded by ANXA3, a suitable minimum fold-change is about 1.6 fold, and a suitable range of fold-changes is about 1.6 to about 11.5 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by CLEC4D, a suitable minimum fold-change is which is about 1.4 fold, and a suitable range of fold-changes is which is about 1.4 to about 15.9 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by LMNB1, a suitable minimum fold-change is about 1.3 fold, and a suitable range of fold-changes is about 1.3 to about 7.0 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by PRRG4, a suitable minimum fold-change is about 1.5 fold, and a suitable range of fold-changes is about 1.5 to about 6.3 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by TNFAIP6, a suitable minimum fold-change is about 1.4 fold, and a suitable range of fold-changes is about 1.45 to about 16.8 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by VNN1, a suitable minimum fold-change is about 1.5 fold, and a suitable range of fold-changes is about 1.45 to about 23.6 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by IL2RB, a suitable maximum fold-change is about 0.8 fold, and a suitable range of fold-changes is about 0.8 to about 0.1 fold, relative to an average level of RNA encoded by the housekeeping gene in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by ANXA3 normalized to IL2RB, a suitable minimum fold-change is about 1.7 fold, and a suitable range of fold-changes is about 1.7 to about 20.7 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by CLEC4D normalized to IL2RB, a suitable minimum fold-change is which is about 1.5 fold, and a suitable range of fold-changes is which is about 1.5 to about 12.0 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by LMNB1 normalized to IL2RB, a suitable minimum fold-change is about 1.5 fold, and a suitable range of fold-changes is about 1.5 to about 10.6 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by PRRG4 normalized to IL2RB, a suitable minimum fold-change is about 1.3 fold, and a suitable range of fold-changes is about 1.3 to about 13.1 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by TNFAIP6 normalized to IL2RB, a suitable minimum fold-change is about 1.5 fold, and a suitable range of fold-changes is about 1.5 to about 16.4 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

For levels of RNA encoded by VNN1 normalized to IL2RB, a suitable minimum fold-change is about 1.3 fold, and a suitable range of fold-changes is about 1.3 to about 11.9 fold, relative to an average level of RNA encoded by IL2RB in blood of subjects not having any colorectal pathology.

As used herein, the term "about" refers to a variability of plus or minus 10 percent.

Thus, a test subject of the invention is classified as being more likely to have colorectal cancer than to not have colorectal cancer if, for each marker gene of the particular set of marker genes of the invention used to practice the method of classifying of the invention, the fold-change in level of RNA encoded by that gene in blood of the test subject relative to blood of the control subjects not having any colorectal cancer pathology classifies, according to the teachings of the invention, the test subject as being more likely to have colorectal cancer than to not have colorectal cancer.

Conversely, a test subject of the invention is classified as being more likely to not have colorectal cancer than to have colorectal cancer if, for each marker gene of the particular set of marker genes of the invention used to practice the method of classifying of the invention, the fold-change in level of RNA encoded by that gene in blood of the test subject relative to blood of the control subjects not having any colorectal cancer pathology does not classify, according to the teachings of the invention, the test subject as being more likely to have colorectal cancer than to not have colorectal cancer.

In one aspect of the invention, the set of one or more colorectal cancer marker genes may consist of any one of the possible combinations of one or more of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 (indicated in Table 6, where each logistic regression model is based on one particular gene combination, and each gene of the combination is assigned a logistic regression coefficient value).

Sets of marker genes of the invention which consist of one or more of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 which can be used to practice the invention include: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, VNN1; ANXA3, CLEC4D, IL2RB, PRRG4; ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4; ANXA3, CLEC4D, IL2RB, PRRG4, VNN1; ANXA3, IL2RB, LMNB1, PRRG4, VNN1; ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6; ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6; ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6; ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6, VNN1; ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ANXA3, IL2RB, LMNB1, PRRG4; IL2RB, PRRG4, VNN1; ANXA3, IL2RB, PRRG4, VNN1; CLEC4D, IL2RB, PRRG4, VNN1; IL2RB, LMNB1, PRRG4, VNN1; CLEC4D, IL2RB, LMNB1, PRRG4, VNN1; ANXA3, IL2RB, PRRG4, TNFAIP6; IL2RB, PRRG4, TNFAIP6, VNN1; ANXA3, IL2RB, PRRG4, TNFAIP6, VNN1; CLEC4D, IL2RB, PRRG4, TNFAIP6, VNN1; IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; IL2RB, PRRG4; ANXA3, IL2RB, PRRG4; CLEC4D, IL2RB, PRRG4; IL2RB, LMNB1, PRRG4; CLEC4D, IL2RB, LMNB1, PRRG4; IL2RB, PRRG4, TNFAIP6; CLEC4D, IL2RB, PRRG4, TNFAIP6; IL2RB, LMNB1, PRRG4, TNFAIP6; CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6; ANXA3, IL2RB, VNN1; ANXA3, CLEC4D, IL2RB, VNN1; ANXA3, IL2RB, LMNB1, VNN1; ANXA3, CLEC4D, IL2RB, LMNB1, VNN1; ANXA3, CLEC4D, LMNB1, PRRG4, VNN1; ANXA3, IL2RB, TNFAIP6, VNN1; ANXA3, CLEC4D, IL2RB, TNFAIP6, VNN1; ANXA3, IL2RB, LMNB1, TNFAIP6, VNN1; ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6, VNN1; ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6, VNN1; ANXA3, IL2RB; ANXA3, CLEC4D, IL2RB; ANXA3, IL2RB, LMNB1; ANXA3, CLEC4D, IL2RB, LMNB1; ANXA3, CLEC4D, LMNB1, PRRG4; CLEC4D, IL2RB, LMNB1, VNN1; ANXA3, IL2RB, TNFAIP6; ANXA3, CLEC4D, IL2RB, TNFAIP6; ANXA3, IL2RB, LMNB1, TNFAIP6; ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6; ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6; IL2RB, LMNB1, TNFAIP6, VNN1; CLEC4D, IL2RB, LMNB1, TNFAIP6, VNN1; IL2RB, LMNB1, VNN1; ANXA3, LMNB1, PRRG4, VNN1; ANXA3, LMNB1, PRRG4, TNFAIP6, VNN1; ANXA3, CLEC4D, PRRG4; ANXA3, LMNB1, PRRG4; CLEC4D, IL2RB, VNN1; ANXA3, CLEC4D, PRRG4, VNN1; IL2RB,

LMNB1, TNFAIP6; CLEC4D, IL2RB, LMNB1, TNFAIP6; ANXA3, CLEC4D, PRRG4, TNFAIP6; ANXA3, LMNB1, PRRG4, TNFAIP6; IL2RB, TNFAIP6, VNN1; CLEC4D, IL2RB, TNFAIP6, VNN1; ANXA3, CLEC4D, PRRG4, TNFAIP6, VNN1; IL2RB, LMNB1; CLEC4D, IL2RB, LMNB1; IL2RB, VNN1; ANXA3, CLEC4D, LMNB1, VNN1; ANXA3, CLEC4D, LMNB1, TNFAIP6, VNN1; ANXA3, CLEC4D, LMNB1; ANXA3, PRRG4; ANXA3, CLEC4D, VNN1; ANXA3, LMNB1, VNN1; ANXA3, PRRG4, VNN1; ANXA3, CLEC4D, LMNB1, TNFAIP6; ANXA3, PRRG4, TNFAIP6; ANXA3, CLEC4D, TNFAIP6, VNN1; ANXA3, LMNB1, TNFAIP6, VNN1; ANXA3, PRRG4, TNFAIP6, VNN1; ANXA3; ANXA3, CLEC4D; ANXA3, LMNB1; ANXA3, VNN1; ANXA3, TNFAIP6; ANXA3, CLEC4D, TNFAIP6; IL2RB, TNFAIP6; CLEC4D, IL2RB, TNFAIP6; ANXA3, LMNB1, TNFAIP6; ANXA3, TNFAIP6, VNN1; CLEC4D, IL2RB; PRRG4, VNN1; CLEC4D, PRRG4, VNN1; LMNB1, PRRG4, VNN1; CLEC4D, LMNB1, PRRG4, VNN1; PRRG4, TNFAIP6, VNN1; CLEC4D, PRRG4, TNFAIP6, VNN1; LMNB1, PRRG4, TNFAIP6, VNN1; CLEC4D, LMNB1, PRRG4, TNFAIP6, VNN1; PRRG4; CLEC4D, PRRG4; LMNB1, PRRG4; CLEC4D, LMNB1, PRRG4; PRRG4, TNFAIP6; CLEC4D, PRRG4, TNFAIP6; LMNB1, PRRG4, TNFAIP6; CLEC4D, LMNB1, PRRG4, TNFAIP6; LMNB1, TNFAIP6, VNN1; CLEC4D, VNN1; LMNB1, VNN1; CLEC4D, LMNB1, VNN1; LMNB1, TNFAIP6; LMNB1, TNFAIP6; TNFAIP6, VNN1; CLEC4D, TNFAIP6, VNN1; CLEC4D, LMNB1, TNFAIP6, VNN1; LMNB1; CLEC4D, LMNB1; VNN1; CLEC4D, TNFAIP6; TNFAIP6; CLEC4D; and IL2RB.

According to the aspect of the invention where the set of one or more colorectal cancer marker genes consists of any one of the 127 possible combinations of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, the level of RNA encoded by a gene of the invention in blood of a subject of the invention may be determined as a ratio to a level of RNA encoded by a housekeeping gene in blood of the subject. It will be appreciated that such measurement of a level or RNA encoded by a gene relative to that of a housekeeping gene within individual samples can be used to control for sample to sample variability.

The housekeeping gene may be any one of various genes expressed in blood known to the ordinarily skilled artisan. In one aspect of the method, the housekeeping gene is ACTB. Alternately, the housekeeping gene may encode 18S rRNA.

Nucleotide sequences of target genes of the invention (ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1) are described in Figures 1A-H and in Table

1, below.

In another aspect of the invention, the set of one or more colorectal cancer marker genes may consist of any one of the possible combinations of one or more of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 (indicated in Table 5, where each logistic regression model is based on one particular gene combination, and each gene of the combination is assigned a logistic regression coefficient value).

The possible combinations of one or more of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 which can be used to practice the invention include: ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1; ANXA3, LMNB1, PRRG4, TNFAIP6 and VNN1; ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6; ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1; ANXA3, PRRG4, TNFAIP6 and VNN1; CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1; ANXA3, PRRG4 and TNFAIP6; CLEC4D, LMNB1, PRRG4 and TNFAIP6; ANXA3, CLEC4D, PRRG4, TNFAIP6 and VNN1; ANXA3, CLEC4D, PRRG4 and TNFAIP6; ANXA3, LMNB1, PRRG4 and VNN1; ANXA3, LMNB1, PRRG4 and TNFAIP6; CLEC4D, LMNB1, PRRG4 and VNN1; ANXA3, CLEC4D, LMNB1, PRRG4; ANXA3, CLEC4D, PRRG4 and VNN1; LMNB1, PRRG4 and VNN1; LMNB1, PRRG4, TNFAIP6 and VNN1; LMNB1, PRRG4 and TNFAIP6; ANXA3, CLEC4D and PRRG4; ANXA3, LMNB1 and PRRG4; ANXA3 and PRRG4; ANXA3, PRRG4 and VNN1; CLEC4D, LMNB1 and PRRG4; LMNB1 and PRRG4; CLEC4D, PRRG4, TNFAIP6 and VNN1; CLEC4D, PRRG4 and TNFAIP6; CLEC4D, PRRG4 and VNN1; CLEC4D and PRRG4; PRRG4, TNFAIP6 and VNN1; PRRG4 and VNN1; PRRG4 and TNFAIP6; PRRG4; TNFAIP6 and VNN1; VNN1; ANXA3, TNFAIP6 and VNN1; ANXA3, LMNB1, TNFAIP6 and VNN1; LMNB1, TNFAIP6 and VNN1; CLEC4D, TNFAIP6 and VNN1; ANXA3, CLEC4D, TNFAIP6 and VNN1; ANXA3, CLEC4D, LMNB1, TNFAIP6 and VNN1; CLEC4D, LMNB1, TNFAIP6 and VNN1; ANXA3 and VNN1; ANXA3, CLEC4D, LMNB1 and TNFAIP6; CLEC4D, LMNB1 and TNFAIP6; CLEC4D and VNN1; LMNB1 and VNN1; ANXA3, CLEC4D and VNN1; ANXA3, LMNB1 and VNN1; ANXA3, LMNB1 and TNFAIP6; LMNB1 and TNFAIP6; CLEC4D, LMNB1 and VNN1; ANXA3, CLEC4D, LMNB1 and VNN1; ANXA3, CLEC4D and TNFAIP6; CLEC4D and TNFAIP6; CLEC4D, LMNB1; ANXA3, CLEC4D and LMNB1; LMNB1; ANXA3 and TNFAIP6; ANXA3 and LMNB1; TNFAIP6; ANXA3 and CLEC4D; CLEC4D; and ANXA3.

According to the aspect of the invention where the set of one or more colorectal cancer marker genes consists of any one of the 63 possible combinations of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the level of RNA encoded by a gene of the invention in blood of a subject of the invention may be determined as a ratio to a level of RNA encoded by IL2RB in blood of the subject.

It will be appreciated that data representing levels of RNA encoded by a set of genes of the invention may be combined with data representing levels of gene products of other genes which are differently expressed in blood in subjects having colorectal cancer relative to subjects not having any colorectal pathology so as to determine a probability that a test subject has colorectal cancer versus not having any colorectal pathology.

In another aspect, the method further comprises determining levels of RNA encoded by the gene in blood of a population of control human subjects having colorectal cancer, and/or in blood of a population of human control subjects not having colorectal cancer, to thereby provide the positive control data and/or the negative control data, respectively. Alternately, it is envisaged that the level of RNA encoded by a gene of the invention in control subjects of the invention could be provided by prior art data corresponding to control data of the invention.

The method of the invention may be practiced using any one of various types of control subjects.

In an aspect of the method of the invention, the control subjects not having colon cancer are subjects having been diagnosed as not having any colorectal pathology as a result of colonoscopic examination. As is described in the Examples section which follows, the method of the invention may be practiced using subjects not having any colorectal pathology as the control subjects not having colorectal cancer.

In an aspect of the method of the invention, the control subjects having colorectal cancer are subjects having been diagnosed as having colorectal cancer as a result of colonoscopic examination. As is described in the Examples section which follows, the method of the invention may be practiced using subjects diagnosed as not having any colorectal pathology as the control subjects not having colorectal cancer.

The method of the invention may furthermore be practiced using any one of various numbers of control subjects. One of ordinary skill in the art will possess the necessary expertise to select a sufficient number of control subjects so as to obtain control data having a desired statistical significance for practicing the method of the invention with a desired level of reliability.

For example, the method of the invention can be practiced using 10 or more, 20 or more, 30 or more, 40 or more, 50 or more, 60 or more, 70 or more, 80 or more, 90 or more, 100 or more, 10 or more, 20 or more, 30 or more, 40 or more, 50 or more, 60 or more, 70 or more, 80 or more, 90 or more, 100 or more, 110 or more, 120 or more, 130 or more, 140 or more, 150 or more, 160 or more, 170 or more, 180 or more, 190 or more, or 200 or more of control subjects having colorectal cancer and/or of control subjects not having colorectal cancer.

In one aspect of the invention, the level of RNA encoded by a gene of the invention in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. As is described in the Examples section, below, the method can be practiced where the level of RNA encoded by a gene of the invention in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. Alternately, it is envisaged that the level of a gene of the invention in blood of a test subject of the invention and in blood of control subjects of the invention could be determined using different methods. It will be appreciated that use of the same method to determine the levels of RNA encoded by a gene of the invention in a test subject and in control subjects of the invention can be used to avoid method-to-method calibration to minimize any variability which might arise from use of different methods.

In one aspect of the method, determining of the level of RNA encoded by a gene of the invention in blood of a subject of the invention is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the subject. Alternately, it is envisaged that determining of the level of RNA encoded by the gene in blood of a subject of the invention could be effected by determining the level of RNA encoded by the gene in an *in-vivo* sample using a suitable method for such a purpose.

In one aspect of the method, the level of RNA encoded by a gene of the invention in blood of a subject of the invention is determined in a sample of RNA isolated from blood of the subject. Alternately, it is envisaged that the level of RNA of a gene of the invention in blood of a subject of the invention could be determined in a sample which includes RNA of blood of the subject but from which RNA has not been isolated therefrom, using a suitable method for such a purpose.

Any one of various methods routinely employed in the art for isolating RNA from blood may be used to isolate RNA from blood of a subject of the invention, so as to enable practicing of the method of the invention.

In one aspect of the method, the level of RNA encoded by a gene of the invention in blood of a subject of the invention is determined in RNA of a sample of whole blood. Any one of various methods routinely employed in the art for isolating RNA from whole blood may be employed for practicing the method.

Alternately, it is envisaged that the level of RNA encoded by a gene of the invention in blood of a subject of the invention could be determined in RNA of a sample of fraction of blood which expresses the gene sufficiently specifically so as to enable the method. Examples of such blood fractions include preparations of isolated types of leukocytes, preparations of isolated peripheral blood mononuclear cells, preparations of isolated granulocytes, preparations of isolated whole leukocytes, preparations of isolated specific types of leukocytes, plasma-depleted blood, preparations of isolated lymphocytes, and the plasma fraction of blood.

In one aspect of the method, isolation of RNA from whole blood of a subject of the invention is effected by using a PAXgene Blood RNA Tube (obtainable from PreAnalytiX) in accordance with the instructions of the PAXgene Blood RNA Kit protocol. As is described in the Examples section below, the method of the invention may be practiced by determining a level of a gene of the invention in RNA isolated from blood from test and control subjects of the invention using PAXgene Blood RNA Tubes.

Determining of a level of RNA encoded by a gene of the invention in a sample of the invention may be effected in any one of various ways routinely practiced in the art.

For example, the level of RNA encoded by a gene of the invention in a sample of the invention may be determined via any one of various methods based on quantitative polynucleotide amplification which are routinely employed in the art for determining a level of RNA encoded by a gene in a sample.

Alternately, the level of RNA encoded by a gene of the invention may be determined via any one of various methods based on quantitative polynucleotide hybridization to an immobilized probe which are routinely employed in the art for determining a level of RNA encoded by a gene in a sample.

In one aspect of the method of the invention, the method based on quantitative polynucleotide amplification used to determine the level of RNA encoded by a gene of the invention is quantitative reverse transcriptase-polymerase chain reaction (PCR) analysis. Any one of various types of quantitative reverse transcriptase-PCR analyses routinely employed in the art to determine the level of RNA encoded by a gene in a sample may be used to practice the invention. For example, any one of various sets of primers may be used to perform quantitative reverse transcriptase-PCR analysis so as to practice the method of the invention.

In one aspect of the method of the invention, the quantitative reverse transcriptase-PCR analysis used to determine the level of RNA encoded by a gene of the invention is quantitative real-time PCR analysis of DNA complementary to RNA encoded by the gene using a labeled probe capable of specifically binding amplification product of DNA complementary to RNA encoded by the gene. For example, quantitative real-time PCR analysis may be performed using a labeled probe which comprises a polynucleotide capable of selectively hybridizing with a sense or antisense strand of amplification product of DNA complementary to RNA encoded by the gene. Labeled probes comprising a polynucleotide having any one of various nucleic acid sequences capable of specifically hybridizing with amplification product of DNA complementary to RNA encoded by the gene may be used to practice the method of the invention.

Quantitative real-time PCR analysis of a level of RNA encoded by a gene of the invention may be performed in any one of various ways routinely employed in the art.

In one aspect of the method of the invention, quantitative real-time PCR analysis is performed by analyzing complementary DNA prepared from RNA of blood a subject of the invention, using the QuantiTect™ Probe RT-PCR system (Qiagen, Valencia, CA; Product Number 204345), a TaqMan dual labelled probe, and a Real-Time PCR System 7500 instrument (Applied Biosystems). As is described in the Examples section which follows, such quantitative real-time PCR analysis may be used to practice the method of the invention.

As specified above, the level of RNA encoded by a gene of the invention may be determined via a method based on quantitative polynucleotide hybridization to an immobilized probe.

In one aspect, determining of the level of RNA encoded by a gene of the invention via a method based on quantitative polynucleotide hybridization is effected using a microarray, such as an Affymetrix U133Plus 2.0 GeneChip oligonucleotide array (Affymetrix; Santa Clara, CA).

As specified above, the level of RNA encoded by a gene of the invention in a sample of the invention may be determined via quantitative reverse transcriptase-PCR analysis using any one of various sets of primers and labeled probes to amplify and quantitate DNA complementary to RNA encoded by a marker gene of the invention produced during such analysis. Examples of suitable primers for use in quantitative reverse transcriptase-PCR analysis of the level of RNA encoded by a target gene of the invention are listed in Table 19. This table further lists examples of suitable polynucleotides comprised in labeled probes for practicing quantitative real-time PCR analysis according to the method of the invention.

Table 19. PCR primers and matching polynucleotides of labeled probes for quantitative PCR analysis.

Gene encoding amplified cDNA	**Assay reagent**	**Nucleic acid sequences of PCR primers and matching polynucleotides comprised in labeled probes**	**Primer / probe position**	**Amplicon size (bp)**
ACTB	5' primer 3' primer probe	5'-CACCACACCTTCTACAATGAGCTG-3' (SEQ ID NO: 1) 5'-ACAGCCTGGATAGCAACGTACA-3' (SEQ ID NO: 2) 5'-AACCGCGAGAAGATGACCCAGATCAT-3' (SEQ ID NO: 3)	259 416 343	158
	5' primer 3' primer probe	5'- ACCTTCTACAATGAGCTGCG-3' (SEQ ID NO: 4) 5'- GGTCTCAAACATGATCTGGGTC-3' (SEQ ID NO: 5) 5'- AAGGCCAACCGCGAGAAGAT-3' (SEQ ID NO: 6)	337 450 409	114
	5' primer 3' primer probe	5'- CACCCAGCACAATGAAGATC-3' (SEQ ID NO: 7) 5'- CTGCTTGCTGATCCACATCT-3' (SEQ ID NO: 8) 5'- ATCATTGCTCCTCCTGAGCG-3' (SEQ ID NO: 9)	1034 1152 1057	119
ANXA 3	5' primer 3' primer probe	5'-GAAACATCTGGTGACTTCCG-3' (SEQ ID NO: 10) 5'-TCTGGGCATCTTGTTTGG-3' (SEQ ID NO: 11) 5'-TTGACTTTGGCAGATGGCAGA-3' (SEQ ID NO: 12)	748 850 778	103
	5' primer 3' primer probe	5'-GGAACAAACGAAGATGCCTTG-3' (SEQ ID NO: 13) 5'-AAGTCACCAGATGTTTCGGA-3' (SEQ ID NO: 14) 5'-ATCTTAACTACCAGGACAAGCAGGCA-3' (SEQ ID NO: 15)	628 764 655	137
	5' primer 3' primer probe	5'-CTACCAGGACAAGCAGGCAA-3' (SEQ ID NO: 16) 5'-TTCTGCCATCTGCCAAAGT-3' (SEQ ID NO: 17) 5'-TCCGAAACATCTGGTGACTTCC-3' (SEQ ID NO: 18)	662 799 745	138
CLEC4	5'	5'-CCATTTAACCCACGCAGAG-3' (SEQ ID NO: 19)	673	101

D	primer 3' primer probe	5'-CAGGCCCATTTATCTTGGTT-3' (SEQ ID NO: 20) 5'-CTGGCATAAGAATGAACCCGACA-3' (SEQ ID NO: 21)	773 696	
	5' primer 3' primer probe	5'-TCCGAAACATCTGGTGACTTCC-3' (SEQ ID NO: 22) 5'-TCCTTTCACTCTCAGCCCAC-3' (SEQ ID NO: 23) 5'-ATGACCATCAGCACGGAAGC-3' (SEQ ID NO: 24)	406 523 550	118
	5' primer 3' primer probe	5'-GGGCTGAGAGTGAAAGGAAC-3' (SEQ ID NO: 25) 5'-CCACTGACCTTTGGCATTC-3' (SEQ ID NO: 26) 5'-ATGACCATCAGCACGGAAGC-3' (SEQ ID NO: 27)	506 654 550	149
IL2RB	5' primer 3' primer probe	5'-AAATCTCCCAAGCCTCCCA-3' (SEQ ID NO: 28) 5'-AGGCAGATCCATTCCTGCT-3' (SEQ ID NO: 29) 5'-TTGAAAGACACCTGGAGTTCG-3' (SEQ ID NO: 30)	588 714 612	127
	5' primer 3' primer probe	5'-GACCCACAGATGCAACATAAG-3' (SEQ ID NO: 31) 5'-GCTTCTGCTTGAGAGTCAGC-3' (SEQ ID NO: 32) 5'-AAATCTCCCAAGCCTCCCAC-3' (SEQ ID NO: 33)	562 698 588	137
	5' primer 3' primer probe	5'-TGGAGACCCACAGATGCAA-3' (SEQ ID NO: 34) 5'-GCTTCTGCTTGAGAGTCAGC-3' (SEQ ID NO: 35) 5'-AAATCTCCCAAGCCTCCCAC-3' (SEQ ID NO: 36)	558 698 588	141
LMNB 1	5' primer 3' primer probe	5'-GGAGTGGTTGTTGAGGAAGAA-3' (SEQ ID NO: 37) 5'-CTGAGAAGGCTCTGCACTGTA-3' (SEQ ID NO: 38) 5'-AACCCCAAGAGCATCCAATAG-3' (SEQ ID NO: 39)	2051 2201 2089	151
	5' primer 3' primer probe	5'-CTGGCGAAGATGTGAAGGT-3' (SEQ ID NO: 40) 5'-CTTCCTCAACAACCACTCCA-3' (SEQ ID NO: 41) 5'-AATTCTCAGGGAGAGGAGGTTG-3' (SEQ ID NO: 42)	1935 2069 1964	135
	5' primer 3' primer probe	5'-AGGCGAAGAAGAGAGGTTGAAG-3' (SEQ ID NO: 43) 5'-CCGCTTTCCTCTAGTTGTACG-3' (SEQ ID NO: 44) 5'-TGTCTCCAAGCCCTTCTTCC-3' (SEQ ID NO: 45)	1513 1615 1536	103
PRRG 4	5' primer 3' primer	5'-ATGCGGGAGAAGAAGTGTTTAC-3' (SEQ ID NO: 46) 5'-CTCTGGCTTCCTCATAATTGC-3' (SEQ ID NO: 47) 5'-CTCTTCACTCCCGGCAACCTAGAA-3' (SEQ ID NO:	341 493 427	153

	probe	48)		
	5' primer	5'-TGCTGCTGGAGTATTTTTGG-3' (SEQ ID NO: 49)	618	130
	3' primer	5'-AATGATGGAGGGAGTGTGC-3' (SEQ ID NO: 50)	747	
	probe	5'-AACATCCATGCTCTTCAGCC-3' (SEQ ID NO: 51)	693	
	5' primer	5'-ACTCCCGGCAACCTAGAAAG-3' (SEQ ID NO: 52)	433	176
	3' primer	5'-GTCAGAAGGCCCATAACATCTA-3' (SEQ ID NO: 53)	608	
	probe	5'-AACGATTGCATTTTGGCAGG-3' (SEQ ID NO: 54)	517	
TNFAIP6	5' primer	5'-GCCTATTGCTACAACCCACA-3' (SEQ ID NO: 55)	448	84
	3' primer	5'-TGGGAAGCCTGGAGATTTA-3' (SEQ ID NO: 56)	531	
	probe	5'-AAGGAGTGTGGTGGCGTCTTTAC-3' (SEQ ID NO: 57)	472	
	5' primer	5'-CAGGTTGCTTGGCTGATTATG-3' (SEQ ID NO: 58)	632	172
	3' primer	5'-TTGATTTGGAAACCTCCAGC-3' (SEQ ID NO: 59)	803	
	probe	5'-TGGCTTTGTGGGAAGATACTGTGG-3' (SEQ ID NO: 60)	684	
	5' primer	5'-CATTAGACTCAAGTATGGTCAGCG-3' (SEQ ID NO: 61)	567	142
	3' primer	5'-TCCACAGTATCTTCCCACAAAG-3' (SEQ ID NO: 62)	708	
	probe	5'-CAGGTTGCTTGGCTGATTATGT-3' (SEQ ID NO: 63)	632	
VNN1	5' primer	5'-TGACAGGAAGTGGCATCTAT-3' (SEQ ID NO: 64)	835	147
	3' primer	5'-TACTGCTGGCATAGGAAGTC-3' (SEQ ID NO: 65)	981	
	probe	5'-AGAAGAGGGAAAACTCCTCCTCTCG-3' (SEQ ID NO: 66)	896	
	5' primer	5'-CTGGAGAATTTCAGGTGTCA-3' (SEQ ID NO: 67)	1360	111
	3' primer	5'-ATGCCCAGTCCTTCTCATAC-3' (SEQ ID NO: 68)	1470	
	probe	5'-ACTGACGGACGCTTGTTTAGTCTGA-3' (SEQ ID NO: 69)	1380	
	5' primer	5'-GTATTCCCAACAGCTTGGAT-3' (SEQ ID NO: 70)	711	144
	3' primer	5'-ATAGATGCCACTTCCTGTCA-3' (SEQ ID NO: 71)	854	
	probe	5'-CATGAGGGTCAATTTCCTTGCATC-3' (SEQ ID NO: 72)	785	

Determining the level of RNA encoded by the marker gene of the invention as a ratio to a housekeeping gene may be effected in any one of various ways routinely employed in the art for determining a ratio of a level of RNA encoded by one gene to a level of RNA encoded by a housekeeping gene, such as ACTB.

In one aspect of the method, determining the level of RNA encoded by the gene of the invention as a ratio to the housekeeping gene is effected via duplex quantitative reverse transcriptase-PCR analysis of RNA encoded by the gene and of RNA encoded by the housekeeping gene in a sample of the invention. Such "duplex quantitative reverse transcriptase PCR analysis" refers to quantitative reverse transcriptase-PCR analysis where DNA complementary to RNA encoded by the gene of the invention and DNA complementary to RNA encoded by the housekeeping gene are co-amplified in the same sample/reaction mixture.

DNA complementary to RNA encoded by the housekeeping gene may be amplified via quantitative reverse transcriptase-PCR analysis using any one of various suitable primers.

In one aspect, the primers may be selected so as to include a primer having a nucleotide sequence which is complementary to a region of a target cDNA template, where the region spans a splice junction joining a pair of exons. It will be appreciated that such a primer can be used to facilitate amplification of DNA complementary to messenger RNA, i.e. mature spliced RNA.

In one aspect of the method, where the housekeeping gene is ACTB, the primers used to amplify DNA complementary to RNA encoded by the housekeeping gene may include a primer having a nucleotide sequence identified as SEQ ID NO: 1, a primer having a nucleotide sequence identified as SEQ ID NO: 2, or both primers.

In another aspect of the method, the level of RNA encoded by the housekeeping gene in blood of the test subject is determined via quantitative reverse transcriptase-PCR analysis, using a labeled probe which comprises a polynucleotide capable of hybridizing to a sense or antisense strand of the amplification product of the DNA complementary to RNA encoded by the housekeeping gene.

In one aspect of the method where the housekeeping gene is ACTB and where the level of RNA encoded by the housekeeping gene in blood of the test subject is determined via quantitative reverse transcriptase-PCR analysis using a primer having a nucleotide sequence identified as SEQ ID NO: 1, and a primer having a nucleotide sequence identified as SEQ ID NO: 2, and a labeled probe, the probe comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 3.

As is demonstrated in Example 2 of the Examples section which follows, the method of the invention can be practiced by determining the level of RNA encoded by any one of the marker genes ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 as a ratio to a level of RNA encoded by ACTB in blood of a subject of the invention, where the level is determined via duplex quantitative reverse transcriptase-PCR analysis using a primer having a nucleotide sequence identified as SEQ ID NO: 1, a primer having a nucleotide sequence identified as SEQ ID NO: 2, and a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 3.

Determining the level of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 or VNN1 as a ratio to IL2RB may be effected in any one of various ways.

In one aspect of the method, determining the level of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 or VNN1 as a ratio to a level of RNA encoded by IL2RB in a sample of the invention is effected via duplex quantitative reverse transcriptase-PCR analysis of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 or VNN1 and of RNA encoded by IL2RB in the sample. Such "duplex quantitative reverse transcriptase PCR analysis" refers to quantitative reverse transcriptase-PCR analysis where DNA complementary to RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 or VNN1 and DNA complementary to RNA encoded by IL2RB are co-amplified in the same sample/reaction mixture.

As described above, following the step of obtaining the test data, the method of the invention comprises the step of determining the probability that the test data corresponds to the positive control data and not to the negative control data.

It will be appreciated that the probability that the test subject does not have any colorectal pathology as opposed to having colorectal cancer can be readily determined from the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. For example, when expressing the probability that the test subject has colorectal cancer as a percentage probability, the probability that the test subject does not have any colorectal pathology as opposed to having colorectal cancer corresponds to 100 percent minus the probability that the test subject does not have any colorectal pathology as opposed to having colorectal cancer.

Determining the probability that the test data corresponds to the positive control data and not to the negative control data may be effected in any one of various ways known to the ordinarily skilled artisan for determining the probability that a gene expression profile of a test subject corresponds to a gene expression profile of of subjects having a pathology and not to a gene expression profile of subjects not having the pathology, where the gene expression profiles of the subjects having the pathology and the subjects not having the pathology are significantly different.

In one aspect of the method, determining the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data.

Various suitable mathematical models which are well known in the art of medical diagnosis using disease markers may be employed to classify a test subject as more likely to have colorectal cancer than to not have colorectal cancer, to determine a probability that a test subject is likely to have colorectal cancer as opposed to not having colorectal cancer, or to diagnose a test subject as having colorectal cancer according to the teachings of the invention. Generally these mathematical models can be unsupervised methods performing a clustering whilst supervised methods are more suited to classification of datasets. (refer, for example, to: Dreiseitl S, Ohno-Machado L. Logistic regression and artificial neural network classification models: a methodology review. J Biomed Inform. 2002 Oct-Dec;35(5-6):352-9; Pepe MS. The Statistical Evaluation of Medical Tests for Classification and Prediction. Oxford, England: Oxford University Press; 2003; Dupont WD. Statistical Modeling for Biomedical Researchers. Cambridge, England: Cambridge University Press; 2002; Pampel FC. Logistic regression: A Primer. Publication # 07-132, Sage Publications: Thousand Oaks, CA. 2000; King EN, Ryan TP. A preliminary investigation of maximum likelihood logistic regression versus exact logistic regression. Am Statistician 2002;56:163-170; Metz CE. Basic principles of ROC analysis. Semin Nucl Med 1978;8:283-98; Swets JA. Measuring the accuracy of diagnostic systems. Science 1988;240:1285-93; Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. Clin Chem 1993;39:561-77; Witten IH, Frank Eibe. Data Mining: Practical Machine Learning Tools and Techniques (second edition). Morgan Kaufman 2005; Deutsch JM. Evolutionary algorithms for finding optimal gene sets in microarray prediction. Bioinformatics 2003;19:45-52; Niels Landwehr, Mark Hall and Eibe Frank (2003) Logistic Model Trees . pp 241-252 in Machine Learning: ECML 2003: 14th European Conference on Machine Learning, Cavtat-Dubrovnik, Croatia, September 22-26, 2003, Proceedings .Publisher: Springer-Verlag GmbH, ISSN: 0302-9743). Examples of such mathematical models, related to learning machine , include: Random Forests methods, logistic regression methods, neural network methods, k-means methods, principal component analysis methods, nearest neighbour classifier analysis methods, linear discriminant analysis ,methods , quadratic discriminant analysis methods, support vector machine methods, decision tree methods, genetic algorithm methods, classifier optimization using bagging methods, classifier optimization using boosting methods, classifier optimization using the Random Subspace methods, projection pursuit methods, genetic programming and weighted voting methods.

In one aspect of the invention, the model used is a logistic regression model. As is described in the Examples section below, logistic regression models can be used according to the method of the invention to determine the probability a test subject of the invention has colorectal cancer as opposed to not having any colorectal pathology. Logistic regression models may also be referred to in the art as "logistic models", and "logit models".

Any one of various particular cases of logistic regression models may be used, for any given set of genes of the invention, for determining the probability that the test data corresponds to the positive control data and not to the negative control data.

In one aspect of the method, determining the probability that the test data corresponds to the positive control data and not to the negative control data is effected by using one or more of the logistic regression models disclosed in Example 2, Example 3 and Example 6.

It will be appreciated that a computer may be used for determining the probability that the test subject has colorectal cancer using a mathematical model, according to the method of the invention.

One of skill in the art will know of suitable mathematical formulas for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher or lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer.

For example, a suitable formula, is one which generates a value representing the ratio of the level of RNA encoded by the gene in blood of the test subject to the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. A ratio of greater than 1 indicates that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and a ratio of less than 1 indicates that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. A formula for generating such a ratio value may have the form:

Value = [level of RNA encoded by the gene in blood of the test subject] /

[level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer]

Alternately, a suitable formula is one which subtracts the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer from the level of RNA encoded by the gene in blood of the test subject, to generate a value representing the difference between the level of RNA encoded by the gene in blood of the test subject from the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. A difference having a positive value indicates that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and a difference having a negative value indicates that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. A formula for generating such a difference value may have the form:

Value = [level of RNA encoded by the gene in blood of the test subject] – [level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer]

Thus, according to another aspect of the invention there is provided a computer-based method of determining the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer. The method is effected by causing a computer to apply to the test data a mathematical model according to the invention, and to output the probability, to thereby enable a determination of the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

Application of computers for determining a probability that a test subject has a disease as opposed to not having the disease, so as to enable the method of the invention, is routinely practiced in the art using computer systems, and optionally computer-readable media, routinely used in the art.

Thus, according to a further aspect of the invention there is provided a computer system for providing the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. The computer system comprises a processor; and a memory configured with instructions that cause the processor to provide a user with the probability, where the instructions comprise applying a mathematical model of the invention to test data of the invention, to thereby determine the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

The instructions may be provided to the computer in any one of various ways routinely employed in the art. In one aspect, the instructions are provided to the computer using a computer-readable medium.

Thus, according to yet another aspect of the invention there is provided a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying a mathematical model of the invention to test data of the invention from, thereby determine the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer.

As described above, following the step of obtaining the test data, the method of classifying of the invention comprises the step of comparing test data representing a level of RNA encoded by a marker gene of the invention to negative control data representing a level of RNA encoded by the gene in subjects not having any colorectal pathology, and determining the fold-change between the levels.

It will be appreciated that a computer may be used for comparing test data representing a level of RNA encoded by a marker gene of the invention to negative control data representing a level of RNA encoded by the gene in subjects not having any colorectal pathology, and determining the fold-change between the levels, according to methods of the invention.

Thus, according to another aspect of the invention there is provided a computer-based method of of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer. The method is effected by using a computer to apply to test data from a test subject according to the invention, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, or lower, for IL2RB, than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. For ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

Application of computers for provide a classification of a test subject as more likely to have a disease than to not have the disease, so as to enable the method of the invention, is routinely practiced in the art using computer systems, and optionally computer-readable media, routinely used in the art.

Thus, according to a further aspect of the invention there is provided a computer system for providing a classification that a test subject is more likely to have colorectal cancer than to not have colorectal cancer. The computer system comprises a processor; and a memory configured with instructions that cause the processor to provide a user with the classification, where the instructions comprise causing the processor to apply to test data, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value representing a fold-change between the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer where, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, a value indicating that the level of RNA encoded by the gene in blood of the test subject is higher, for example within a range of suitable fold-changes taught herein, than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, a value indicating that the level of RNA encoded by the gene in blood of the test subject is lower, for example within a range of suitable fold-changes disclosed herein, than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

The instructions may be provided to the computer in any one of various ways routinely employed in the art. In one aspect, the instructions are provided to the computer using a computer-readable medium.

Thus, according to yet another aspect of the invention there is provided a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying to test data and to negative control data representing a level of RNA encoded by a marker gene of the invention in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value representing the fold-change between the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, a value indicating that the level of RNA encoded by the gene in blood of the test subject is higher, for example, within a suitable range of fold-changes disclosed herein, than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, a value indicating that the level of RNA encoded by the gene in blood of the test subject is lower, for example, within a suitable range of fold-changes disclosed herein, than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

Thus, according to still yet another aspect of the invention there is provided a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying, to test data representing a level of RNA encoded by the gene in blood of a human test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

An exemplary computer system for practicing certain of the methods described herein is described in Figure 1.

Figure 1 shows a schematic of a general-purpose computer system 100 suitable for practicing the methods described herein. The computer system 100, shown as a self-contained unit but not necessarily so limited, comprises at least one data processing unit (CPU) 102, a memory 104, which will typically include both high speed random access memory as well as non-volatile memory (such as one or more magnetic disk drives) but may be simply flash memory, a user interface 108, optionally a disk 110 controlled by a disk controller 112, and at least one optional network or other communication interface card 114 for communicating with other computers as well as other devices. At least the CPU 102, memory 104, user interface 108, disk controller where present, and network interface card, communicate with one another via at least one communication bus 106.

Memory 104 stores procedures and data, typically including: an operating system 140 for providing basic system services; application programs 152 such as user level programs for viewing and manipulating data, evaluating formulae for the purpose of diagnosing a test subject; authoring tools for assisting with the writing of computer programs; a file system 142, a user interface controller 144 for handling communications with a user via user interface 108, and optionally one or more databases 146 for storing data of the invention and other information, optionally a graphics controller 148 for controlling display of data, and optionally a floating point coprocessor 150 dedicated to carrying out mathematical operations. The methods of the invention may also draw upon functions contained in one or more dynamically linked libraries, not shown in Figure 1, but stored either in Memory 104, or on disk 110, or accessible via network interface connection 114.

User interface 108 may comprise a display 128, a mouse 126, and a keyboard 130. Although shown as separate components in Figure 1, one or more of these user interface components can be integrated with one another in embodiments such as handheld computers. Display 128 may be a cathode ray tube (CRT), or flat-screen display such as an LCD based on active matrix or TFT embodiments, or may be an electroluminescent display, based on light emitting organic molecules such as conjugated small molecules or polymers. Other embodiments of a user interface not shown in Figure 1 include, e.g., several buttons on a keypad, a card-reader, a touch-screen with or without a dedicated touching device, a trackpad, a trackball, or a microphone used in conjunction with voice-recognition software, or any combination thereof, or a security-device such as a fingerprint sensor or a retinal scanner that prohibits an unauthorized user from accessing data and programs stored in system 100.

System 100 may also be connected to an output device such as a printer (not shown), either directly through a dedicated printer cable connected to a serial or USB port, or wirelessly, or via a network connection.

The database 146 may instead, optionally, be stored on disk 110 in circumstances where the amount of data in the database is too great to be efficiently stored in memory 104. The database may also instead, or in part, be stored on one or more remote computers that communicate with computer system 100 through network interface connection 114.

The network interface 134 may be a connection to the internet or to a local area network via a cable and modem, or ethernet, firewire, or USB connectivity, or a digital subscriber line. Preferably the computer network connection is wireless, e.g., utilizing CDMA, GSM, or GPRS, or bluetooth, or standards such as 802.11a, 802.11b, or 802.11g.

It would be understood that various embodiments and configurations and distributions of the components of system 10 across different devices and locations are consistent with practice of the methods described herein. For example, a user may use a handheld embodiment that accepts data from a test subject, and transmits that data across a network connection to another device or location where the data is analyzed according to a formulae described herein. A result of such an analysis can be stored at the other location and/or additionally transmitted back to the handheld embodiment. In such a configuration, the act of accepting data from a test subject can include the act of a user inputting the information. The network connection can include a web-based interface to a remote site at, for example, a healthcare provider. Alternatively, system 10 can be a device such as a handheld device that accepts data from the test subject, analyzes the data, such as by inputting the data into a formula as further described herein, and generating a result that is displayed to the user. The result can then be, optionally, transmitted back to a remote location via a network interface such as a wireless interface. System 100 may further be configured to permit a user to transmit by e-mail results of an analysis directly to some other party, such as a healthcare provider, or a diagnostic facility, or a patient.

In one aspect of the invention there is provided a method of determining whether a subject is at an increased risk of having colorectal cancer relative to the general population. The method comprises obtaining a test biological sample of blood from the subject; for each of a set of genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, determining the amount of RNA encoded by the gene in the test biological sample; comparing the determined amount of RNA for each these genes with the amount in one or more control biological samples of blood; and concluding or determining that the subject is at increased risk, average risk or decreased risk of having colorectal cancer relative to the general population if the amount of RNA encoded by each gene in the test biological sample is higher than in the control biological samples for genes ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and lower for IL2RB.

A test subject would be considered as being at "increased risk" of having or developing colorectal cancer if the amount of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and/or VNN1 present in the test biological sample is higher than that seen in the control samples to an approximate extent (plus or minus 10%) seen in the working examples herein. A test subject would be considered as being at "increased risk" of having or developing colorectal cancer if the amount of RNA encoded by IL2RB present in the test biological sample is lower than that seen in the control samples to an approximate extent (plus or minus 10%) seen in the working examples herein.

A combination of marker genes of the invention, such as ANXA3, CLEC4D, LMNB1, PRRG4, VNN1, and IL2RB, can be used together with the known CRC prevalence rate to determine useful thresholds for stratifying the probability of having colorectal cancer in an average risk population. Using the combined training/blind set (IL2RB duplex) described in the Examples, an increased probability threshold can be selected to identify a sub-population with a colorectal cancer occurrence rate of 1.5%, a 3-fold increase over the base disease prevalence rate; this threshold reflects the same relative risk associated with having a first degree relative with colorectal cancer. A decreased probability threshold reflecting a sensitivity for colorectal cancer detection of, for example, 80%, 75%, 70%, 65%, can be selected to identify a lower-than-average probability sub-population. This approach can be used to stratify patients into an increased probability group, a decreased probability, and an average probability group.

One of ordinary skill in the art will be able to determine directly from the literature, or will be able to calculate from available statistical data, a suitable prevalence rate of colorectal cancer for practicing embodiments of the invention. For example, the prevalence rate for colorectal cancer in the average risk population over 50 years of age has been determined to be 0.7% (see for example Imperiale TF. *et al.*, 2004. Colorectal Cancer Study Group. Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. New Engl J Med 351:2704-14).

It will be appreciated that components for practicing quantitative PCR according to the method of the invention may be assembled in a kit.

Thus, according to still another aspect of the invention there is provided a kit. The kit comprises packaging and contains, for each gene of a set of two or more of the following target genes of the invention: ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1; a primer set capable of generating an amplification product of DNA complementary to RNA encoded, in a human subject, only by the gene.

In various aspects of the kit of the invention, the set of genes may be any combination of two or more of the target genes of the invention, as described hereinabove and in the Examples section, below.

In one aspect of the invention, the kit further contains two or more of the following components: a thermostable polymerase, a reverse transcriptase, deoxynucleotide triphosphates, nucleotide triphosphates and enzyme buffer.

In another aspect of the invention, the kit further contains at least one labeled probe capable of selectively hybridizing to either a sense or an antisense strand of the amplification product.

In yet another aspect of the invention, the kit further contains a computer-readable medium of the invention.

In one aspect, the kit is identified in print in or on the packaging as being for determining a probability that a test subject has colorectal cancer, for example, a probability that a test subject has colorectal cancer as opposed to not having colorectal cancer.

In another aspect, the kit is identified in print in or on the packaging as being for classifying a test subject as being more likely to have colorectal cancer than to not have colorectal cancer, and/or as being more likely to not have colorectal cancer than to have colorectal cancer.

In a further aspect, the kit is identified in print in or on the packaging as being for determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population

In various aspects of the kit of the invention, the set of genes may be any combination of two or more of the target genes of the invention.

Sets of genes of the invention which consist of two or more of ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 include: ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, IL2RB,

LMNB1, PRRG4, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, PRRG4; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4; ACTB, ANXA3, CLEC4D, IL2RB, PRRG4, VNN1; ACTB, ANXA3, IL2RB, LMNB1, PRRG4, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6; ACTB, ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6; ACTB, ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, IL2RB, LMNB1, PRRG4; ACTB, IL2RB, PRRG4, VNN1; ACTB, ANXA3, IL2RB, PRRG4, VNN1; ACTB, CLEC4D, IL2RB, PRRG4, VNN1; ACTB, IL2RB, LMNB1, PRRG4, VNN1; ACTB, CLEC4D, IL2RB, LMNB1, PRRG4, VNN1; ACTB, ANXA3, IL2RB, PRRG4, TNFAIP6; ACTB, IL2RB, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, IL2RB, PRRG4, TNFAIP6, VNN1; ACTB, CLEC4D, IL2RB, PRRG4, TNFAIP6, VNN1; ACTB, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, IL2RB, PRRG4; ACTB, ANXA3, IL2RB, PRRG4; ACTB, CLEC4D, IL2RB, PRRG4; ACTB, IL2RB, LMNB1, PRRG4; ACTB, CLEC4D, IL2RB, LMNB1, PRRG4; ACTB, IL2RB, PRRG4, TNFAIP6; ACTB, CLEC4D, IL2RB, PRRG4, TNFAIP6; ACTB, IL2RB, LMNB1, PRRG4, TNFAIP6; ACTB, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6; ACTB, ANXA3, IL2RB, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, VNN1; ACTB, ANXA3, IL2RB, LMNB1, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, VNN1; ACTB, ANXA3, CLEC4D, LMNB1, PRRG4, VNN1; ACTB, ANXA3, IL2RB, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, TNFAIP6, VNN1; ACTB, ANXA3, IL2RB, LMNB1, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, IL2RB; ACTB, ANXA3, CLEC4D, IL2RB; ACTB, ANXA3, IL2RB, LMNB1; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1; ACTB, ANXA3, CLEC4D, LMNB1, PRRG4; ACTB, CLEC4D, IL2RB, LMNB1, VNN1; ACTB, ANXA3, IL2RB, TNFAIP6; ACTB, ANXA3, CLEC4D, IL2RB, TNFAIP6; ACTB, ANXA3, IL2RB, LMNB1, TNFAIP6; ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6; ACTB, ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6; ACTB, IL2RB, LMNB1, TNFAIP6, VNN1; ACTB, CLEC4D, IL2RB, LMNB1, TNFAIP6, VNN1; ACTB, IL2RB, LMNB1, VNN1; ACTB, ANXA3, LMNB1, PRRG4, VNN1; ACTB, ANXA3, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, PRRG4; ACTB, ANXA3, LMNB1, PRRG4; ACTB, CLEC4D, IL2RB, VNN1; ACTB, ANXA3, CLEC4D, PRRG4, VNN1; ACTB, IL2RB, LMNB1, TNFAIP6; ACTB, CLEC4D, IL2RB, LMNB1, TNFAIP6; ACTB,

ANXA3, CLEC4D, PRRG4, TNFAIP6; ACTB, ANXA3, LMNB1, PRRG4, TNFAIP6; ACTB, IL2RB, TNFAIP6, VNN1; ACTB, CLEC4D, IL2RB, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, PRRG4, TNFAIP6, VNN1; ACTB, IL2RB, LMNB1; ACTB, CLEC4D, IL2RB, LMNB1; ACTB, IL2RB, VNN1; ACTB, ANXA3, CLEC4D, LMNB1, VNN1; ACTB, ANXA3, CLEC4D, LMNB1, TNFAIP6, VNN1; ACTB, ANXA3, CLEC4D, LMNB1; ACTB, ANXA3, PRRG4; ACTB, ANXA3, CLEC4D, VNN1; ACTB, ANXA3, LMNB1, VNN1; ACTB, ANXA3, PRRG4, VNN1; ACTB, ANXA3, CLEC4D, LMNB1, TNFAIP6; ACTB, ANXA3, PRRG4, TNFAIP6; ACTB, ANXA3, CLEC4D, TNFAIP6, VNN1; ACTB, ANXA3, LMNB1, TNFAIP6, VNN1; ACTB, ANXA3, PRRG4, TNFAIP6, VNN1; ACTB, ANXA3; ACTB, ANXA3, CLEC4D; ACTB, ANXA3, LMNB1; ACTB, ANXA3, VNN1; ACTB, ANXA3, TNFAIP6; ACTB, ANXA3, CLEC4D, TNFAIP6; ACTB, IL2RB, TNFAIP6; ACTB, CLEC4D, IL2RB, TNFAIP6; ACTB, ANXA3, LMNB1, TNFAIP6; ACTB, ANXA3, TNFAIP6, VNN1; ACTB, CLEC4D, IL2RB; ACTB, PRRG4, VNN1; ACTB, CLEC4D, PRRG4, VNN1; ACTB, LMNB1, PRRG4, VNN1; ACTB, CLEC4D, LMNB1, PRRG4, VNN1; ACTB, PRRG4, TNFAIP6, VNN1; ACTB, CLEC4D, PRRG4, TNFAIP6, VNN1; ACTB, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, CLEC4D, LMNB1, PRRG4, TNFAIP6, VNN1; ACTB, PRRG4; ACTB, CLEC4D, PRRG4; ACTB, LMNB1, PRRG4; ACTB, CLEC4D, LMNB1, PRRG4; ACTB, PRRG4, TNFAIP6; ACTB, CLEC4D, PRRG4, TNFAIP6; ACTB, LMNB1, PRRG4, TNFAIP6; ACTB, CLEC4D, LMNB1, PRRG4, TNFAIP6; ACTB, LMNB1, TNFAIP6, VNN1; ACTB, CLEC4D, VNN1; ACTB, LMNB1, VNN1; ACTB, CLEC4D, LMNB1, VNN1; ACTB, LMNB1, TNFAIP6; ACTB, LMNB1, TNFAIP6; ACTB, TNFAIP6, VNN1; ACTB, CLEC4D, TNFAIP6, VNN1; ACTB, CLEC4D, LMNB1, TNFAIP6, VNN1; ACTB, LMNB1; ACTB, CLEC4D, LMNB1; ACTB, VNN1; ACTB, CLEC4D, TNFAIP6; ACTB, TNFAIP6; ACTB, CLEC4D; and ACTB, IL2RB.

In one aspect of the kit of the invention, the set of one or more genes consists of a housekeeping gene such as ACTB, and one or more of the colorectal cancer marker genes: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and ANXA3.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and CLEC4D.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and IL2RB.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and LMNB1.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and PRRG4.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and TNFAIP6.

In one aspect of the kit of the invention, the set of one or more genes consists of ACTB and VNN1.

In another aspect of the kit of the invention, the set of one or more genes consists of IL2RB, and one or more of the colorectal cancer marker genes: ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and ANXA3.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and CLEC4D.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and LMNB1.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and PRRG4.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and TNFAIP6.

In one aspect of the kit of the invention, the set of one or more genes consists of IL2RB and VNN1.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 1, and a primer having a nucleotide sequence identified as SEQ ID NO: 2.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 1, and a primer having a nucleotide sequence identified as SEQ ID NO: 2 and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 3.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 10, and a primer having a nucleotide sequence identified as SEQ ID NO: 11.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 10, and a primer having a nucleotide sequence identified as SEQ ID NO: 11, and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 12.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 19, and a primer having a nucleotide sequence identified as SEQ ID NO: 20.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 19, and a primer having a nucleotide sequence identified as SEQ ID NO: 20 and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 21.

In one aspect of the invention, for example, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 28, and a primer having a nucleotide sequence identified as SEQ ID NO: 29.

In one aspect of the invention, for example, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 28, and a primer having a nucleotide sequence identified as SEQ ID NO: 29 and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 30.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 37, and a primer having a nucleotide sequence identified as SEQ ID NO: 38.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 37, and a primer having a nucleotide sequence identified as SEQ ID NO: 38 and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 39.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 46, and a primer having a nucleotide sequence identified as SEQ ID NO: 47.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 46, and a primer having a nucleotide sequence identified as SEQ

ID NO: 47, and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 48.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 55, and a primer having a nucleotide sequence identified as SEQ ID NO: 56.

In one aspect of the invention, the kit contains a primer having a nucleotide sequence identified as SEQ ID NO: 55, and a primer having a nucleotide sequence identified as SEQ ID NO: 56 and the kit further contains a labeled probe which comprises a polynucleotide having a nucleic acid sequence identified as SEQ ID NO: 57.

Further, non-limiting, specific aspects of the invention include the following:

One aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising: the steps of (a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of (a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of (a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of: (a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of: (a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of: (a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising the steps of: (a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

An embodiment of aspects of the invention disclosed herein includes that the determining of the level of RNA encoded by the gene in blood of the test subject be effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject. An embodiment of aspects of the invention disclosed herein includes the further step of determining the levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. An embodiment of aspects of the invention disclosed herein includes that the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of aspects of the invention disclosed herein includes that the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of aspects of the invention disclosed herein includes that the determining of the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data, and where the mathematical model is for determining the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data. An embodiment of aspects of the invention disclosed herein includes that the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. An aspect of this latter embodiment includes that the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of aspects of the invention disclosed herein includes that the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. An aspect of this latter embodiment includes that the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

An aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: inputting, to a computer, test data representing a level of RNA encoded by a CLEC4D gene in blood of the test subject; and causing the computer to apply to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: inputting, to a computer, test data representing a level of RNA encoded by a IL2RB gene in blood of the test subject; and causing the computer to apply to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

An embodiment of the invention's computer based methods includes where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of computer based methods of the invention includes where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of each of computer based methods of the invention includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. An embodiment of computer based methods of the invention includes where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of each of the computer based methods of the invention includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. In a further embodiment the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

Another aspect of the invention disclosed herein is a method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: comprising the steps of: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) determining a probability that the test data corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. An embodiment of this aspect of the invention disclosed herein is where the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject. An embodiment of this aspect of the invention disclosed herein further comprises determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. An embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of this aspect of the invention disclosed herein is where the determining of the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data, and where the mathematical model is for determining the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data. An embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. In a further embodiment, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. In a further embodiment, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

Another aspect of the invention disclosed herein is a computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by the gene in blood of the test subject, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, computer-implemented steps of: (a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and (b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. In an embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. In an embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. In an embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. In a further embodiment of this aspect of the invention disclosed herein is where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. In an embodiment of this aspect of the invention disclosed herein is where the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. In a further embodiment of this aspect of the invention disclosed herein, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB. In an embodiment of this aspect of the invention disclosed herein is where the set of one or more genes consists of PRRG4. In an embodiment of this aspect of the invention disclosed herein is where the set of one or more genes consists of IL2RB and PRRG4.

Another aspect of the invention disclosed herein is a kit comprising packaging and containing, for each gene of a set of two or more genes selected from the group consisting of ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, a primer set capable of generating an amplification product of DNA complementary to RNA encoded, in a human subject, only by the gene. An embodiment of this aspect of the invention disclosed herein is where the kit further contains two or more components selected from the group consisting of a thermostable polymerase, a reverse transcriptase, deoxynucleotide triphosphates, nucleotide triphosphates and enzyme buffer. An embodiment of this aspect of the invention disclosed herein is where the kit further contains at least one labelled probe capable of selectively hybridizing to either a sense or an antisense strand of the amplification product. An embodiment of this aspect of the invention disclosed herein is where the kit further contains a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying a mathematical model to test data representing a level of RNA encoded by the gene in blood of a human test subject, where the mathematical model is derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, and where the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of the kit consists of ACTB and one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and ANXA3. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and CLEC4D. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and IL2RB. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and LMNB1. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and PRRG4. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and TNFAIP6. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of ACTB and VNN1. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and ANXA3. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of\ IL2RB and CLEC4D. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and LMNB1. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and PRRG4. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and TNFAIP6. An embodiment of this aspect of the invention disclosed herein is where the set of one or more genes of one or more genes of the kit consists of IL2RB and VNN1.

Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:(a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising: (a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:(a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

An embodiment of the methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer of the invention includes determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject. An embodiment of the invention's methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer of the invention includes further determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. An embodiment of the invention's methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer of the invention includes where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of the invention's methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer of the invention includes where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of the invention's methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer of the invention includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. In an aspect of this embodiment, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of the invention's methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject, and/or where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a CLEC4D gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a IL2RB gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a LMNB1 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a PRRG4 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a TNFAIP6 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by a VNN1 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (b) outputting the value, where an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

An embodiment of the invention's computer-based methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, includes where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of the invention's computer-based methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, includes where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of the invention's computer-based methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. An aspect of this embodiment includes where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of the invention's computer-based methods of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. An aspect of this embodiment includes where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

Another aspect of the invention disclosed herein is a method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1: (a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data; (b) providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and (c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. An embodiment of this aspect includes determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject. Another embodiment of this aspect includes further comprising determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer. Anther embodiment of this aspect includes where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. An embodiment of this aspect includes where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. An embodiment of this aspect includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. An further embodiment includes where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. An embodiment of this aspect includes where the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. An embodiment of this aspect includes where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

Another aspect of the invention disclosed herein is a computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, computer-implemented steps of: (a) applying to test data representing a level of RNA encoded by the gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a formula for calculating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, where, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and where, for IL2RB, an indication that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer. An embodiment of this aspect of the invention disclosed herein includes where the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis. Another embodiment of this aspect of the invention disclosed herein includes where the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method. Another embodiment of this aspect of the invention disclosed herein includes where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject. In a further embodiment of this embodiment of the invention as disclosed herein is where the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB. Another embodiment of this aspect of the invention disclosed herein includes where the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and where the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject. In a further embodiment of this embodiment of the invention as disclosed herein, the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB. In a further embodiment of this embodiment of the invention as disclosed herein, the set of one or more genes consists of PRRG4. In a further embodiment of this embodiment of the invention as disclosed herein, the set of one or more genes consists of IL2RB and PRRG4.

Another aspect of the invention disclosed herein is a kit comprising packaging and containing, for each gene of a set of two or more genes selected from the group consisting of ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, a primer set capable of generating an amplification product of DNA complementary to RNA encoded, in a human subject, only by the gene. In an embodiment of this aspect of the invention disclosed herein, the kit further containing two or more components selected from the group consisting of a thermostable polymerase, a reverse transcriptase, deoxynucleotide triphosphates, nucleotide triphosphates and enzyme buffer. In another embodiment of this aspect of the invention disclosed herein, the kit further contains at least one labelled probe capable of selectively hybridizing to either a sense or an antisense strand of the amplification product. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and ANXA3. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and CLEC4D. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and IL2RB. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and LMNB1. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and PRRG4. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and TNFAIP6. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of ACTB and VNN1. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists IL2RB and ANXA3. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and CLEC4D. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and LMNB1. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and PRRG4. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and TNFAIP6. In another embodiment of this aspect of the invention disclosed herein, the set of one or more genes of the kit consists of IL2RB and VNN1.

Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a annexin A3 (ANXA3) gene in the test sample of blood, (ii) comparing the level of RNA encoded by ANXA3 as determined in step (i) with a level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a C-type lectin domain family 4, member D (CLEC4D) gene in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a interleukin 2 receptor, beta (IL2RB) gene in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a lamin B1 (LMNB1) gene in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a proline rich Gla (G carboxyglutamic acid) 4 (transmembrane) (PRRG4) gene in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a tumor necrosis factor, alpha induced protein 6 gene (TNFAIP6) in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and (i) determining a level of RNA encoded by a vanin 1 (VNN1) gene in the test sample of blood, (ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood. In an embodiment of any one of these eight aspects these methods of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, the control samples are from individuals who have been diagnosed as not having colorectal cancer.

Another aspect of the invention disclosed herein is a method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising: (a) obtaining a test sample of blood from the subject; and for each gene of a set of genes selected from the group consisting of : ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, (i) determining a level of RNA encoded by the gene in the test sample of blood, thereby generating test data; and (ii) applying to the test data and to control data representing a level of RNA encoded by the gene in one or more control samples of blood a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and, for IL2RB, whether the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood; and (b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the value indicates that the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for IL2RB, the value indicates that the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a CLEC4D gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a PRRG4 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and TNFAIP6, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an CLEC4D gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a PRRG4, gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. Another aspect of the invention disclosed herein is an isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. One embodiment of this composition further comprises a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and TNFAIP6, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a CLEC4D gene, or composition thereof.

Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an LMNB1 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof. Another aspect of the invention disclosed herein is a primer set comprising a first primer, where the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, and a second primer, where the second primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

Another aspect of the invention disclosed herein is test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a CLEC4D, gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA

Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a PRRG4 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. Another aspect of the invention disclosed herein is a test system comprising: a) two or more blood samples where each blood sample is from a different test subject, and b) an isolated nucleic acid molecule of each the blood sample from a test subject, where the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA. An embodiment of any of the test systems described in this paragraph includes where the test subject is being screened for colorectal cancer.

The following non-limiting examples are illustrative of the invention:

EXAMPLES

EXAMPLE 1

General materials and methods

Introduction: The following materials and methods describe experiments performed to demonstrate that analysis of blood for levels of RNA encoded by genes surprisingly identified by the present inventors as colorectal cancer marker genes in blood via array hybridization analysis using an Affymetrix U133Plus 2.0 GeneChip oligonucleotide array (Affymetrix; Santa Clara, CA) (data not shown), can also serve as blood markers for diagnosing colorectal cancer via quantitative reverse-transcriptase PCR analysis.

Blood sample collection: Samples of 2.5 ml whole blood were collected into PAXgene Blood RNA Tubes (PreAnalytiX) from human subjects not having any colorectal pathology and from human subjects having colorectal cancer. Samples were obtained from subjects enrolled in colorectal cancer studies conducted by GeneNews Corp. and collaborating institutions. Blood samples from subjects having colorectal cancer were collected prior to tumor resection, and cancer stage and histology were determined by institutional pathologists. Blood samples from subjects not having any colorectal pathology were collected from subjects presenting for endoscopy screening. Informed consent was obtained according to the research protocols approved by the research ethical boards of the institutions involved. Experimental group sample pairs were selected with an effort to match gender, age, body mass index (BMI), ethnicity and medical history. Samples were divided into training and test sets.

RNA isolation: A sample of 2.5 ml whole blood was collected into PAXgene Blood RNA tubes (PreAnalytiX) and processed in accordance with the instructions of the PAXgene

Blood RNA Kit protocol. In brief, after storing the blood in the PAXgene tube for at least 2 hours, the blood sample was centrifuged and the supernatant discarded. To the remaining sample, 350 microliters of the supplied Buffer BR1 was added, and the sample was pipetted into the spin column and centrifuged, washed and finally eluted as isolated RNA and stored.

Reverse transcription: Reverse transcription of blood sample-derived RNA into single-stranded complementary DNA was performed using the High Capacity cDNA Reverse Transcription Kit from (Applied Biosystems; Foster City, CA; Product number 4368814), according to the manufacturer's instructions. Specifically, 1 microgram of isolated RNA was incubated with reverse transcriptase buffer, dNTPs, random primers and reverse transcriptase and incubated at 25°C for 10 minutes and subsequently at 37°C for two hours.

Quantitative real time RT-PCR: Quantitative real-time PCR analysis to measure levels of RNA encoded by the genes listed in **Table 1** was performed on cDNA samples using the QuantiTect™ Probe RT-PCR system (Qiagen; Valencia, CA; Product No. 204345), using the primers listed in **Table 2** for amplification of cDNA template corresponding to the indicated gene, and TaqMan dual labelled probes comprising the polynucleotides listed in **Table 3** for measuring levels of amplicon corresponding to the indicated gene. The TaqMan probe and primers were ordered from Applied Biosystems Assays-On-Demand, or from IDT (Integrated DNA Technologies, Coralville, IA), or from Biosearch Technologies (Novato, CA). XXX SPECIFY PROBES USED IN EXAMPLES & PEAmplicon levels were measured in real time using a Real-Time PCR System 7500 instrument (Applied Biosystems). Specifically, 20 nanograms of cDNA resulting from reverse transcription was added to the QuantiTect Probe PCR Master Mix as provided and no adjustments were made for magnesium concentration. Uracil-N-Glycosylase was not added. Both forward primer and reverse primer (Table 1) specific to the target genes were added to a concentration of 5 micromolar, and the resultant 25 microliter reaction volume was incubated as follows: 50 degrees centigrade for 2 minutes, followed by 95 degrees centigrade for 15 minutes, followed by 40 cycles of: [94 degrees centigrade for 15 seconds, followed by 55 degrees centigrade for 35 seconds, followed by 72 degrees centigrade for 30 seconds]. Amplification data was collected during each of the 40 incubations at 55 degrees centigrade. All quantitative reverse transcriptase-PCR analyses were performed as duplex amplifications of a target gene and a reference gene (either ACTB or IL2RB, as indicated) in the same reaction mixture. Serial dilution measurements for target and duplex partner genes were assayed, to ensure that the values were within linear range and that the amplification efficiencies were approximately equal. Examination via polyacrylamide gel electrophoresis provided confirmation of specific PCR amplification and the lack of primer-dimer formation in each reaction well.

Table 1. Genes encoding target RNAs for determining colorectal cancer probability versus absence of colorectal pathology.

Gene Symbol	GenBank Accession	Gene Description
ACTB	NM_001101	beta-actin
ANXA3	NM_005139	annexin A3
CLEC4D	NM_080387	C-type lectin domain family 4, member D
IL2RB	NM_000878	interleukin 2 receptor, beta
LMNB1	NM_005573	lamin B1
PRRG4	NM_024081	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)
TNFAIP6	NM_007115	tumor necrosis factor, alpha-induced protein 6
VNN1	NM_004666	vanin 1

Table 2. Primers used for quantitative PCR analysis.

Gene encoding amplified cDNA	Primer	Primer pair sequences	Primer position	Amplicon size (bp)
ACTB	5' 3'	5'-CACCACACCTTCTACAATGAGCTG-3' (SEQ ID NO: 1) 5'-ACAGCCTGGATAGCAACGTACA-3' (SEQ ID NO: 2)	259 416	158
ANXA3	5' 3'	5'-GAAACATCTGGTGACTTCCG-3' (SEQ ID NO: 10) 5'-TCTGGGCATCTTGTTTGG-3' (SEQ ID NO: 11)	748 850	103
CLEC4D	5' 3'	5'-CCATTTAACCCACGCAGAG-3' (SEQ ID NO: 19) 5'-CAGGCCCATTTATCTTGGTT-3' (SEQ ID NO: 20)	673 773	101
IL2RB	5' 3'	5'-AAATCTCCCAAGCCTCCCA-3' (SEQ ID NO: 28) 5'-AGGCAGATCCATTCCTGCT-3' (SEQ ID NO: 29)	588 714	127
LMNB1	5' 3'	5'-GGAGTGGTTGTTGAGGAAGAA-3' (SEQ ID NO: 37) 5'-CTGAGAAGGCTCTGCACTGTA-3' (SEQ ID NO: 38)	2051 2201	151
PRRG4	5' 3'	5'-ATGCGGGAGAAGAAGTGTTTAC-3' (SEQ ID NO: 46) 5'-CTCTGGCTTCCTCATAATTGC-3' (SEQ ID NO: 47)	341 493	153
TNFAIP6	5' 3'	5'-GCCTATTGCTACAACCCACA-3' (SEQ ID NO: 55) 5'-TGGGAAGCCTGGAGATTTA-3' (SEQ ID NO: 56)	448 531	84
VNN1	5' 3'	5'-TGACAGGAAGTGGCATCTAT-3' (SEQ ID NO: 64) 5'-TACTGCTGGCATAGGAAGTC-3' (SEQ ID NO: 65)	835 981	147

Table 3. TaqMan® probes used for quantitative PCR analysis.

Gene encoding amplicon	Taqman probe base sequence	Probe position
ACTB	5'-AACCGCGAGAAGATGACCCAGATCAT-3' (SEQ ID NO: 3)	343
ANXA3	5'-TTGACTTTGGCAGATGGCAGA-3' (SEQ ID NO: 12)	778
CLEC4D	5'-CTGGCATAAGAATGAACCCGACA-3' (SEQ ID NO: 21)	696
IL2RB	5'-TTGAAAGACACCTGGAGTTCG-3' (SEQ ID NO: 30)	612
LMNB1	5'-AACCCCAAGAGCATCCAATAG-3' (SEQ ID NO: 39)	2089
PRRG4	5'-CTCTTCACTCCCGGCAACCTAGAA-3' (SEQ ID NO: 48)	427
TNFAIP6	5'-AAGGAGTGTGGTGGCGTCTTTAC-3' (SEQ ID NO: 57)	472
VNN1	5'-AGAAGAGGGAAAACTCCTCCTCTCG-3' (SEQ ID NO: 66)	896

Determination of observed range of fold-changes in levels of RNA encoded by marker genes in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology: For each of the sample training and sample test sets, average fold-change in levels of RNA encoded by marker genes, normalized to either ACTB or IL2RB, were calculated as the ratio of average levels of RNA encoded by marker genes in blood of subjects having colorectal cancer to average levels of RNA encoded by marker genes in blood of subjects not having any colorectal pathology. The statistical significance of the fold-changes were confirmed by a p-value of less than 0.05. Maximum observed directional fold-changes in normalized levels of RNA encoded by marker genes found to be higher in blood of subjects having colorectal cancer than in blood of subjects not having any colorectal pathology were further calculated, for each marker gene, as the ratio of the highest level observed in any single sample from a subject having colorectal cancer to the average level in subjects not having any colorectal pathology. Similarly, maximum observed directional fold-changes in normalized levels of RNA encoded by marker genes found to be lower in blood of subjects having colorectal cancer than in blood of subjects not having any colorectal pathology were further calculated, for each marker gene, as the ratio of the lowest level observed in any single sample from a subject having colorectal cancer to the average level in subjects not having any colorectal pathology. In this way, observed ranges of fold-changes, ranging from average fold-change to maximal observed directional fold-change, in levels of RNA encoded by marker genes in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology were determined.

Formulation of mathematical models for determining probability of colorectal cancer versus absence of colorectal pathology: Logistic regression was used to formulate mathematical models for determining the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology. Levels of RNA encoded by colorectal cancer marker genes and of reference genes determined via duplex quantitative reverse transcriptase PCR in blood of positive and negative control subjects were analyzed via logistic regression so as to generate models having the general form:

$P = \{1 + e\text{^}\text{-}[K_0 + K_1L_1 + K_2L_2 + K_3L_3 \ldots + K_nL_n]\}\text{^-}1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology; K_0 is a constant; K_1 is a coefficient specific to a first marker gene; L_1 is a ratio of a level of RNA encoded by the first gene to a level of RNA encoded by a reference gene in blood of the test subject; K_2 is a coefficient specific to a second marker gene; L_2 is a ratio of a level of RNA encoded by the second gene to a level of RNA encoded by the reference gene in blood of the test subject; K_3 is a coefficient specific to a third marker gene; L_3 is a ratio of a level of RNA encoded by the third gene to a level of RNA encoded by the reference gene in blood of the test subject; K_n is a coefficient specific to an nth marker gene; and L_n is a ratio of a level of RNA encoded by the nth gene to a level of RNA encoded by the reference gene in blood of the test subject. The ratio of the level of RNA encoded by a marker gene to the level of RNA encoded by a reference gene was calculated as the change (ΔCt) in the cycle number (Ct) at which the increase in fluorescence is exponential between the marker gene and the reference gene according to the equation: ΔCt = Ct (marker gene) – Ct (reference gene). The caret symbol "^" is used herein to denote that a value preceding the caret is raised to a power corresponding to the value following the caret.

EXAMPLE 2

Measurement of blood levels of RNA encoded by any combination of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and/or VNN1 can be used to determine a probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology

MATERIALS AND METHODS:

Refer to "General materials and methods", above.

EXPERIMENTAL RESULTS:

Sample training set:

Discovery of significantly different levels of RNA encoded by ANXA3, CLEC4D,

IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 and in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology: Quantitative reverse transcriptase PCR analysis of gene expression in a training set of blood samples from 117 subjects having colorectal cancer and 130 subjects not having any colorectal pathology, using the housekeeping gene ACTB as duplex partner for normalization of gene expression levels was performed. The normalized RNA levels measured are shown in Table 4.

Table 4. Sample training set levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by ACTB. Levels shown correspond to ΔCt.

Sample ID	Group	Gene						
		ANXA3	CLEC4D	IL2RB	LMNB1	PRRG4	TNFAIP6	VNN1
CD0011pax	0	6.523	7.755	5.195	7.310	7.860	8.501	8.991
CD0012pax	0	7.878	8.595	5.250	7.525	8.183	8.439	9.878
CD0030pax	0	6.411	6.420	4.173	6.220	6.973	5.901	7.101
CD0063pax	0	7.103	8.545	4.203	7.165	7.795	8.499	8.628
CD0077pax	0	4.808	6.185	5.098	5.405	6.710	6.524	6.533
CD0078pax	0	5.946	7.000	3.553	5.820	5.570	7.476	6.488
CD0085pax	0	5.543	7.700	5.003	6.210	7.460	8.149	6.678
CD0117pax	0	6.021	8.170	4.463	5.685	8.020	8.166	6.573
CD0146pax	0	5.396	6.335	4.468	5.320	5.735	6.691	6.253
CD0167pax	0	3.501	4.893	4.480	4.978	5.590	6.469	5.173
CD0249pax	0	4.443	4.855	4.878	4.803	6.043	5.556	6.471
CD0279pax	0	5.503	7.095	4.270	5.395	6.098	6.694	7.043
CD0286pax	0	4.791	6.928	4.350	5.383	5.960	5.714	5.598
CD0297pax	0	5.861	6.670	5.083	6.565	6.405	6.186	7.118
CD0323pax	0	6.966	7.773	4.645	5.723	7.470	8.149	8.738
CD0445pax	0	6.458	7.420	4.448	6.103	6.448	7.216	7.411
CD0463pax	0	4.391	6.485	4.203	5.605	6.583	6.161	7.036
CD0491pax	0	5.093	6.370	4.928	6.123	6.978	7.171	6.511
CD0496pax	0	6.058	8.270	4.670	6.355	7.783	6.434	6.623
CD0501pax	0	6.326	7.725	4.613	6.270	7.215	8.581	6.978
CD0504pax	0	4.023	5.060	4.858	5.920	7.530	5.289	6.113
CD0573pax	0	6.791	6.140	4.248	6.160	6.713	7.646	7.286
CD0578pax	0	6.328	6.670	4.128	5.128	6.033	6.411	7.081
CD0620pax	0	2.361	3.628	6.120	3.873	6.120	5.274	5.613
CD0639pax	0	5.611	7.013	4.980	6.258	5.630	6.689	7.528
CD0645pax	0	4.596	5.868	5.190	4.908	5.475	6.099	5.608

CD0679pax	0	5.611	7.808	5.070	5.633	6.150	7.974	7.748
CD0685pax	0	5.796	8.150	4.358	6.050	7.155	7.606	6.673
CD0716pax	0	6.961	8.193	4.090	5.648	5.750	6.669	7.388
CD0749pax	0	5.208	6.970	4.520	5.565	6.430	7.176	6.316
CD0760pax	0	2.868	5.020	5.603	3.605	5.790	4.679	5.663
CD0811pax	0	7.188	8.065	3.275	6.500	7.305	6.021	6.141
CD0846pax	0	4.626	6.488	4.730	5.308	5.645	4.864	7.813
CD0848pax	0	5.113	6.235	3.380	5.915	6.388	6.409	7.263
CD0924pax	0	5.731	6.370	5.238	6.095	6.248	5.791	6.131
CD1066pax	0	5.346	5.900	4.903	5.990	6.868	7.466	6.211
CD1073pax	0	5.681	5.813	5.150	5.858	6.350	6.674	6.663
CD1075pax	0	5.128	7.010	4.535	6.075	8.228	7.264	6.563
CD1089pax	0	5.081	7.225	5.733	5.550	6.395	6.546	6.668
CD1116pax	0	4.188	5.500	5.023	5.295	6.180	5.764	6.378
CD1120pax	0	3.663	5.495	5.203	4.780	6.555	6.864	5.118
CD1198pax	0	5.398	6.210	4.155	6.055	6.095	6.086	5.881
PB1179pax	0	6.401	7.293	4.700	6.563	7.080	8.169	7.418
PB1277pax	0	6.403	7.520	4.860	6.260	7.185	7.586	6.351
PB1301pax	0	4.733	6.200	6.268	5.608	6.863	5.891	5.531
PB1315pax	0	3.898	6.165	5.438	4.998	6.008	5.206	7.161
PB1345pax	0	5.246	6.280	4.598	6.410	6.775	6.051	7.663
PB1518pax	0	6.806	7.803	5.055	5.818	7.230	7.134	7.328
PB1520pax	0	4.283	5.560	3.250	4.660	3.793	5.214	6.108
PB1574pax	0	7.538	8.685	5.583	7.453	7.483	7.166	8.226
PB1783pax	0	8.056	9.095	5.453	7.650	8.535	9.011	8.448
PB1799pax	0	7.338	8.760	5.765	7.435	8.855	9.181	7.801
PB1811pax	0	6.848	8.115	5.080	7.140	8.390	7.416	7.471
PB1830pax	0	5.788	7.385	5.923	6.440	6.870	7.444	9.253
PB1833pax	0	5.943	7.620	5.488	6.615	7.620	6.829	8.098
PB1843pax	0	7.218	7.870	5.780	6.770	8.338	5.739	8.708
PB1851pax	0	7.468	8.045	6.050	7.795	8.325	10.181	9.261
PB1919pax	0	8.271	9.525	5.233	7.165	8.975	9.051	9.108
PB1922pax	0	6.788	8.280	6.028	7.363	8.348	9.281	8.306
PB1924pax	0	7.748	8.655	6.758	7.628	8.303	8.816	9.401
PB1937pax	0	7.178	9.085	5.118	7.665	9.740	8.754	8.798
PB1964pax	0	5.491	7.820	4.463	6.065	7.843	7.726	8.496
PB2027pax	0	5.463	6.525	5.150	6.300	7.360	7.401	7.546
PB2029pax	0	5.793	7.060	5.050	6.375	6.973	7.624	7.758
PB2073pax	0	6.021	6.335	4.873	6.290	7.933	6.991	6.846
PB2086pax	0	5.048	5.665	4.208	5.098	6.453	5.286	5.991
PB2099pax	0	4.808	5.360	5.388	5.910	6.680	5.604	7.003
PB2100pax	0	6.353	6.960	4.465	6.085	7.625	7.351	6.826
PB2132pax	0	5.693	7.235	4.438	5.745	6.995	7.649	7.518
PB2168pax	0	6.776	7.593	4.605	6.168	7.125	8.284	6.993
PB2192pax	0	6.701	7.845	5.483	6.230	6.965	7.751	8.378
PB2196pax	0	6.061	7.655	4.573	6.195	7.985	7.781	6.668

PB2200pax	0	6.706	7.640	5.158	6.025	7.103	6.826	6.276
PB2213pax	0	6.898	7.435	4.773	6.380	6.630	8.614	7.448
PB2224pax	0	4.841	5.385	4.743	5.210	6.448	7.546	6.851
PB2228pax	0	6.511	6.915	3.953	6.450	7.373	8.906	8.086
PB2229pax	0	5.771	6.440	5.588	6.030	5.865	7.091	6.528
PB2277pax	0	6.348	6.685	4.290	5.705	5.930	5.986	7.351
PB2297pax	0	5.886	6.785	4.703	5.835	6.533	6.451	5.696
PB2312pax	0	5.533	6.530	3.773	6.098	5.978	6.651	6.746
PB2398pax	0	4.711	5.390	5.033	5.440	5.748	5.136	7.111
PB2409pax	0	5.946	7.195	4.933	5.835	6.950	6.811	7.683
PB2414pax	0	7.843	7.790	3.955	6.380	7.745	9.026	7.101
PB2467pax	0	5.773	6.935	4.260	5.955	6.525	7.596	6.756
PB2473pax	0	6.818	8.275	5.530	7.375	8.405	7.586	8.561
PB2512pax	0	5.603	7.355	4.340	6.215	6.345	6.926	7.511
PB2568pax	0	5.326	5.850	5.303	5.710	7.178	7.561	7.331
PB2571pax	0	5.561	5.995	4.523	6.060	6.173	7.396	7.791
PB2603pax	0	5.778	6.480	3.953	5.903	6.313	7.021	5.986
PB2624pax	0	5.383	5.465	3.948	5.498	6.838	6.146	6.741
PB2824pax	0	5.781	6.748	4.675	5.758	6.830	7.154	7.223
PB2880pax	0	5.906	6.090	4.728	6.160	5.218	7.361	7.386
PB3088pax	0	6.601	6.760	3.858	5.725	6.395	8.456	7.378
RC0882pax	0	5.043	6.540	4.533	5.708	6.083	7.351	7.151
RC0888pax	0	4.726	5.740	4.948	5.330	6.775	6.516	6.168
RC0968pax	0	3.238	3.590	4.008	4.303	6.118	4.716	7.086
RC2114pax	0	4.473	5.900	4.768	5.168	6.028	5.216	7.446
RC2238pax	0	7.318	8.785	5.878	7.175	8.665	9.209	9.903
RC2681pax	0	6.331	7.515	5.623	6.995	7.833	6.471	7.536
RC2703pax	0	8.093	8.360	5.973	7.053	8.253	7.801	8.091
RC2749pax	0	6.448	8.695	5.895	7.205	7.905	7.726	8.666
RC2750pax	0	5.578	6.650	6.753	6.428	7.993	7.761	7.111
RC2756pax	0	7.478	8.135	5.340	7.095	8.420	7.781	8.671
RC2771pax	0	5.848	8.345	6.240	6.440	7.648	8.449	9.303
RC2790pax	0	8.086	9.228	6.880	7.573	8.475	8.679	8.948
RC2792pax	0	7.956	8.058	5.850	7.068	8.320	9.219	8.448
RC2808pax	0	6.556	8.790	5.233	6.605	7.815	7.096	7.653
RC2822pax	0	7.921	9.163	6.255	7.193	8.075	10.284	7.718
RC2834pax	0	6.588	8.535	6.520	6.810	7.920	9.946	9.651
RC2871pax	0	5.443	6.530	4.563	6.280	7.165	7.479	8.158
RC2879pax	0	6.266	8.105	5.978	6.620	8.465	7.971	7.298
RC2892pax	0	6.086	7.423	5.185	6.163	7.185	8.559	7.748
RC2895pax	0	6.148	6.900	4.378	6.270	7.450	6.109	7.473
RC2921pax	0	6.846	7.623	4.720	6.758	7.520	7.954	8.073
RC2958pax	0	6.581	6.735	4.863	6.185	6.638	5.851	7.616
RC3022pax	0	6.401	6.660	4.888	6.685	7.925	7.776	6.578
RC3112pax	0	6.938	8.095	5.408	6.435	7.475	8.629	7.713
RC3146pax	0	6.018	6.655	5.340	5.905	6.855	7.491	7.451

RC3184pax	0	6.998	7.910	4.398	6.370	7.395	7.329	7.598
RC3232pax	0	5.021	6.460	5.003	5.030	7.008	4.941	8.671
RC3324pax	0	5.158	6.220	5.203	5.055	6.935	6.869	5.713
RC3327pax	0	5.238	5.225	4.708	5.313	5.253	6.381	7.541
RC3334pax	0	5.953	7.670	4.710	6.135	6.850	6.816	8.081
RC3355pax	0	5.871	7.253	5.620	5.358	6.325	7.699	6.648
RC3380pax	0	5.418	6.395	5.363	5.453	6.423	6.786	6.481
RC3392pax	0	6.378	8.025	4.445	6.170	7.265	8.546	7.756
RC3413pax	0	6.176	7.940	4.768	6.100	6.545	7.051	8.858
RC3421pax	0	5.661	5.515	5.088	5.900	6.483	5.191	5.961
RC3468pax	0	5.831	5.890	5.443	5.905	6.523	7.171	6.636
RC3498pax	0	5.553	5.515	5.593	6.145	7.200	7.484	6.468
CD0157pax	1	6.223	6.530	4.198	6.115	6.930	7.654	8.168
CD0164pax	1	4.726	5.395	4.083	5.660	10.733	7.791	6.696
CD0256pax	1	4.833	6.295	4.735	6.045	6.785	7.141	6.911
CD0322pax	1	5.153	7.050	6.308	5.820	7.325	7.239	8.603
CD0356pax	1	5.243	5.555	6.038	5.925	6.580	6.239	5.823
CD0371pax	1	5.643	7.110	5.073	6.045	6.245	6.394	5.968
CD0629pax	1	4.453	5.995	4.503	5.555	7.380	5.114	6.563
CD1050pax	1	6.238	5.930	4.943	6.150	7.105	6.969	7.243
MH0001pax	1	7.266	8.375	5.103	7.770	8.568	9.266	8.706
MH0009pax	1	6.078	7.150	5.990	6.325	7.185	6.131	6.426
MH0011pax	1	2.393	4.420	8.808	4.258	6.888	3.846	5.756
MH0012pax	1	4.673	6.965	5.368	5.970	7.680	6.659	7.043
MH0014pax	1	6.266	8.155	5.003	6.395	6.995	9.436	7.983
MH0016pax	1	5.408	6.770	6.225	6.050	6.635	6.181	6.561
MH0017pax	1	6.071	8.290	5.323	6.710	6.750	8.231	8.433
MH0018pax	1	6.856	7.175	5.093	6.250	7.358	8.451	6.791
MH0021pax	1	6.948	6.675	5.263	5.483	6.398	8.236	8.111
MH0022pax	1	6.471	7.508	5.280	6.228	7.030	7.344	7.548
MH0024pax	1	5.016	5.640	4.488	5.340	5.793	5.211	6.241
MH0026pax	1	4.351	6.775	5.558	5.440	6.840	5.861	6.028
MH0028pax	1	6.183	6.815	5.818	5.918	5.883	5.986	6.176
MH0029pax	1	5.388	6.360	5.015	6.255	5.925	6.846	6.831
MH0035pax	1	6.111	8.575	4.708	6.645	7.460	7.051	7.638
MH0037pax	1	5.441	7.063	5.375	5.578	6.325	7.089	7.948
MH0038pax	1	7.206	7.463	5.020	6.748	7.635	8.089	8.113
MH0039pax	1	4.036	5.113	5.110	5.298	5.110	5.394	6.383
MH0042pax	1	4.643	5.560	4.425	5.900	5.785	4.876	5.901
MH0050pax	1	3.763	6.495	4.908	4.718	5.698	6.641	7.721
MH0051pax	1	4.941	5.693	6.225	5.818	4.795	4.044	6.338
PB1829pax	1	7.363	9.380	6.678	7.073	7.428	8.841	9.241
PB1842pax	1	7.483	8.295	6.188	7.488	7.173	8.786	8.011
PB1872pax	1	7.051	8.525	6.318	7.410	7.175	8.486	7.533
PB2857pax	1	4.268	6.600	4.810	5.300	6.470	5.266	6.976
RC2919pax	1	7.106	7.488	4.420	6.463	8.350	8.399	9.318

RC3062pax	1	5.006	6.200	4.513	5.195	6.340	5.271	5.538
RC3277pax	1	5.068	6.360	4.770	5.360	6.205	5.701	6.136
RC3297pax	1	5.748	6.970	4.728	5.843	6.493	8.451	7.206
RC3445pax	1	5.503	6.560	5.290	6.295	6.560	6.711	7.021
RC3467pax	1	6.893	8.640	3.945	6.670	7.040	8.251	7.771
CC0003pax	1	4.281	5.963	5.500	4.608	5.205	7.009	4.853
DC0001pax	1	5.713	5.580	5.378	5.868	6.408	6.201	6.541
DC0002pax	1	6.323	6.125	5.423	6.380	6.410	7.374	7.273
DS0003pax	1	4.816	6.663	6.615	5.248	7.380	6.849	6.398
FC0005pax	1	5.953	6.735	5.618	6.605	6.980	6.649	8.698
FC0011pax	1	6.458	7.550	7.063	6.915	7.950	8.539	8.338
FC0012pax	1	3.868	6.850	7.138	5.285	6.375	6.849	7.063
JGA0001pax	1	5.426	6.250	7.448	6.125	8.173	6.586	7.096
JGA0008pax	1	5.448	7.600	6.018	6.793	7.403	7.366	7.841
JH0002pax	1	6.108	7.335	5.633	6.725	6.950	7.484	7.128
JH0003pax	1	6.053	6.635	5.090	5.905	6.145	5.701	7.081
JH0004pax	1	5.373	5.985	5.265	5.935	6.570	7.371	6.961
JH0005pax	1	5.341	6.565	5.008	5.780	6.688	7.356	7.091
JH0006pax	1	4.771	5.840	5.073	5.525	6.198	6.731	5.551
JH0007pax	1	2.956	3.035	5.353	4.815	6.483	5.661	4.916
JH0008pax	1	5.876	8.435	5.173	6.265	7.573	7.811	6.711
JH0009pax	1	4.101	3.770	4.793	5.540	5.293	4.636	5.876
JH0010pax	1	5.026	5.810	4.958	6.105	7.018	6.046	5.526
JH0012pax	1	4.981	5.435	4.718	5.965	6.318	5.801	6.511
JH0013pax	1	5.501	6.610	5.268	5.905	7.048	8.861	7.191
JH0014pax	1	5.053	5.235	4.253	4.735	4.860	6.259	7.488
JH0016pax	1	5.596	6.390	4.438	5.980	6.338	5.566	6.191
JH0018pax	1	4.401	5.770	5.248	5.765	6.348	5.696	6.446
JH0019pax	1	5.751	6.775	5.468	6.055	6.693	5.926	6.656
JH0020pax	1	5.001	7.450	4.563	5.875	5.618	5.756	6.706
JH0021pax	1	5.726	7.650	6.058	5.730	6.105	6.611	6.808
JH0023pax	1	4.696	6.805	3.873	5.020	6.960	5.951	6.968
JH0024pax	1	6.008	7.895	5.113	6.865	7.620	9.099	8.698
JH0025pax	1	4.796	5.780	5.398	5.150	5.225	5.626	6.423
JH0026pax	1	4.491	6.940	5.363	5.800	6.725	7.646	7.493
JH0027pax	1	3.111	4.720	6.498	4.280	5.225	4.486	5.288
JH0028pax	1	4.416	5.680	3.858	5.395	5.820	7.196	6.378
JH0029pax	1	4.176	5.950	5.063	5.055	5.850	4.971	6.963
JH0031pax	1	5.371	7.385	5.613	6.040	6.595	7.096	7.213
JH0032pax	1	7.326	8.430	4.933	6.075	6.925	8.231	8.408
JH0033pax	1	5.258	8.160	5.380	5.560	6.455	8.126	6.181
JH0034pax	1	4.061	6.560	4.468	5.725	6.135	6.721	6.703
JH0035pax	1	4.051	6.625	3.703	4.690	4.400	6.551	5.523
JH0036pax	1	5.348	6.260	4.608	5.480	6.030	6.904	6.618
JH0038pax	1	4.538	6.195	4.878	5.025	5.945	7.049	5.673
JH0039pax	1	5.458	6.595	4.165	5.525	6.950	8.691	5.141

JH0040pax	1	5.458	6.555	4.773	6.140	6.580	6.144	6.658
JH0041pax	1	6.038	7.940	5.033	6.335	6.760	7.489	7.178
JH0042pax	1	3.191	4.985	5.398	4.500	5.978	4.401	4.221
JH0043pax	1	5.263	6.670	6.073	6.110	5.955	5.779	9.668
JH0046pax	1	5.161	5.360	4.448	5.885	5.808	5.951	5.811
JH0047pax	1	4.396	6.385	4.078	5.625	6.828	6.501	6.836
JH0051pax	1	4.881	6.370	5.158	5.290	5.130	5.676	5.388
JH0052pax	1	5.066	7.240	5.528	5.510	5.625	5.616	5.703
JH0053pax	1	4.653	6.375	5.483	5.258	6.578	5.701	6.571
JH0057pax	1	4.201	7.330	4.208	4.755	6.140	6.661	5.968
JH0059pax	1	3.698	4.950	4.243	4.478	4.668	4.896	5.166
JH0060pax	1	4.733	6.230	5.303	5.833	6.448	6.646	6.861
JH0061pax	1	5.063	7.300	4.298	5.063	6.208	8.041	5.466
JH0063pax	1	4.923	6.845	4.748	5.433	5.178	6.021	7.756
JH0065pax	1	3.263	5.220	5.660	4.510	5.355	4.816	4.301
JH0066pax	1	5.703	7.575	6.638	5.988	5.818	5.851	6.791
JH0068pax	1	5.536	6.448	4.895	5.473	5.925	7.239	7.708
JH0069pax	1	3.723	5.435	4.460	4.800	4.955	4.436	4.061
JH0071pax	1	3.748	4.580	6.050	4.785	5.850	5.096	6.261
JH0072pax	1	5.863	6.185	5.185	6.015	6.035	7.306	6.386
JH0077pax	1	4.473	5.810	5.193	5.635	6.020	5.959	7.278
JH0078pax	1	5.591	5.693	3.685	5.818	4.875	5.419	5.778
JH0080pax	1	2.903	4.470	5.033	4.158	5.093	3.921	6.031
JH0082pax	1	4.611	5.398	4.800	5.108	5.465	5.364	6.683
JH0083pax	1	3.903	6.445	5.398	5.333	4.473	6.006	6.606
JH0086pax	1	5.633	5.850	5.063	5.288	4.978	5.936	7.021
JH0092pax	1	5.241	8.328	5.350	6.113	6.540	6.349	7.663
MIP0004pax	1	3.201	3.098	5.340	3.873	4.510	4.459	2.743
MP0013Apax	1	7.028	9.300	6.195	7.105	8.385	8.561	7.406
MP0014Bpax	1	6.418	8.420	6.623	6.633	8.008	8.746	7.586
MP0018Apax	1	6.003	7.900	7.005	6.740	6.635	7.146	6.281
MP0019Bpax	1	6.283	7.090	6.653	6.528	7.058	6.696	8.656
MP0024pax	1	5.436	7.823	6.375	6.383	7.655	8.939	8.013
NK2001pax	1	5.061	6.843	6.230	5.613	4.680	6.349	7.873
NK2002pax	1	5.516	5.903	5.210	5.568	5.585	6.809	6.753
NK2003pax	1	4.986	6.388	5.590	5.588	6.345	7.404	5.723
NK2004pax	1	4.626	6.648	5.435	5.048	4.945	6.319	5.318

Surprisingly, analysis of the data showed that RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 is present on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology, and that RNA encoded by IL2RB is present on average at a significantly lower level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 5). The ranges of fold-change in the levels of RNA encoded by these genes normalized to levels of RNA encoded by ACTB in blood of the training set subjects having colorectal cancer relative to the training set subjects not having any colorectal pathology are shown in Table 5.

Table 5. Sample training set ranges of fold-changes in levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by ACTB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene						
	ANXA3	**CLEC4D**	**IL2RB**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**
Average normalized RNA level in subjects having colorectal cancer (ΔCt)	5.21	6.58	5.28	5.76	6.41	6.64	6.77
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	5.92	7.02	4.95	6.09	7.00	17.19	7.31
Average RNA level fold-change	1.63	1.36	0.80	1.26	1.51	1.46	1.45
p-value for average RNA level fold-change	5.0E-07	2.6E-03	1.1E-03	5.4E-04	2.3E-06	7.0E-04	1.4E-04
Maximum observed RNA level directional fold-change	11.53	15.86	0.07	4.66	6.07	10.12	23.63

As can be seen in Table 5, a test subject having a blood level of RNA encoded by ANXA3 which is 1.6 to 11.5 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by CLEC4D which is 1.4 to 15.9 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by LMNB1 which is 1.3 to 4.7 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by PRRG4 which is 1.5 to 6.1 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by TNFAIP6 which is 1.46 to 10.12 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by VNN1 which is 1.45 to 23.63 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 5, a test subject having a blood level of RNA encoded by IL2RB which is 0.8 to 0.1 fold that of the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Generation of logistic regression models for determining the probability that a test subject has colorectal cancer versus not having any colorectal pathology via measurement of levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by ACTB: Linear regression analysis of levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 surprisingly showed that logistic regression models based on blood expression levels of all 127 possible combinations of one or more of these genes determined in the sample training set could be generated, for discriminating, with a receiver-operating characteristic (ROC) area under the curve (AUC) of at least 0.61, between subjects having colorectal cancer and subjects not having any colorectal pathology. Examples of these logistic regression models are shown in Table 6. A model based on ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 (Table 6, Model #1) was surprisingly found to enable discrimination with a ROC AUC of 0.79 between subjects having colorectal cancer and subjects not having any colorectal pathology.

By way of example, Model # 1 of Table 6 corresponds to:

$P = \{1 + e^{\wedge}\text{-}[0.684 + (-0.916)(L_{ANXA3}) + (0.353)(L_{CLEC4D}) + (0.871)(L_{IL2RB}) + (0.907)(L_{LMNB1}) + (-0.968)(L_{PRRG4}) + (0.154)(L_{TNFAIP6}) + (-0.355)(L_{VNN1})]\}^{\wedge}\text{-}1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, L_{ANXA3} is a ratio of a level of RNA encoded by ANXA3 to a level of RNA encoded by ACTB in blood of the test subject, L_{CLEC4D} is a ratio of a level of RNA encoded by CLEC4D to a level of RNA encoded by ACTB in blood of the test subject, L_{IL2RB} is a ratio of a level of RNA encoded by IL2RB to a level of RNA encoded by ACTB in blood of the test subject, L_{LMNB1} is a ratio of a level of RNA encoded by LMNB1 to a level of RNA encoded by ACTB in blood of the test subject, L_{PRRG4} is a ratio of a level of RNA encoded by PRRG4 to a level of RNA encoded by ACTB in blood of the test subject, $L_{TNFAIP6}$ is a ratio of a level of RNA encoded by TNFAIP6 to a level of RNA encoded by ACTB in blood of the test subject, and L_{VNN1} is a ratio of a level of RNA encoded by VNN1 to a level of RNA encoded by ACTB in blood of the test subject.

Further by way of example, Model #104 of Table 6 corresponds to:

$P = \{1 + e^{\wedge}\text{-}[4.311 + (-0.659)(L_{PRRG4})]\}^{\wedge}\text{-}1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, and L_{PRRG4} is a ratio of a level of RNA encoded by PRRG4 to a level of RNA encoded by ACTB in blood of the test subject.

Table 6. Logistic regression models based on blood expression levels of any possible combination of one or more of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 for determining the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer. ROC AUC values for the models are shown for the sample training set used to generate the models, as well as for an independent blind sample test set used to test the models. The models, listed in order of decreasing ROC AUC value for the training set, are based on expression levels determined via quantitative reverse transcriptase-PCR analysis using ACTB as duplex partner for normalization. The form of these models is: $P = \{1 + e^{\wedge}\text{-}[K_0 + K_1L_1 + K_2L_2 + K_3L_3\ldots + K_nL_n]\}^{\wedge}\text{-}1$, where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology; K_0 is a constant; K_1 is a coefficient specific to a first gene; L_1 is a ratio of a level of RNA encoded

by the first gene to a level of RNA encoded by ACTB in blood of the test subject; K_2 is a coefficient specific to a second gene; L_2 is a ratio of a level of RNA encoded by the second gene to a level of RNA encoded by ACTB in blood of the test subject; K_3 is a coefficient specific to a third gene; L_3 is a ratio of a level of RNA encoded by the third gene to a level of RNA encoded by ACTB in blood of the test subject; K_n is a coefficient specific to an nth gene; and L_n is a ratio of a level of RNA encoded by the nth gene to a level of RNA encoded by ACTB in blood of the test subject. No regression coefficients are specified for genes which are not included in the gene combination (indicated by "–") on which a given logistic regression model is based.

Logistic regression model #	**No. of genes in model**	**ROC AUC**		**Constant (K_0)**	**Gene-specific regression coefficient (K_n)**						
		Training Set	**Blind Test Set**		**ANXA3**	**CLEC4D**	**IL2RB**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**
1	7	0.79	0.79	0.684	-0.916	0.353	0.871	0.907	-0.968	0.154	-0.355
2	6	0.79	0.79	0.743	-0.859	0.402	0.870	0.893	-0.916	–	-0.341
3	4	0.78	0.78	1.321	-0.614	0.358	0.898	–	-0.749	–	–
4	5	0.78	0.79	0.343	-0.907	0.322	0.829	0.737	-0.925	–	–
5	5	0.78	0.78	1.814	-0.527	0.424	0.943	–	-0.715	–	-0.267
6	5	0.78	0.82	0.830	-0.641	–	0.883	0.935	-0.824	–	-0.270
7	5	0.78	0.79	1.264	-0.658	0.318	0.898	–	-0.788	0.120	–
8	5	0.78	0.82	0.359	-0.825	–	0.845	0.794	-0.927	0.189	–
9	6	0.78	0.80	0.282	-0.953	0.280	0.829	0.740	-0.965	0.123	–
10	6	0.78	0.78	1.772	-0.575	0.380	0.944	–	-0.760	0.141	-0.277
11	6	0.78	0.82	0.727	-0.768	–	0.883	0.948	-0.918	0.230	-0.304
12	4	0.77	0.82	0.477	-0.716	–	0.848	0.803	-0.850	–	–
13	3	0.77	0.80	1.969	–	–	1.001	–	-0.752	–	-0.305
14	4	0.77	0.81	1.950	-0.280	–	0.966	–	-0.610	–	-0.189

15	4	0.77	0.78	1.915	–	0.161	1.009	–	-0.840	–	-0.374
16	4	0.77	0.80	1.686	–	–	0.995	0.238	-0.855	–	-0.363
17	5	0.77	0.79	1.748	–	0.130	1.005	0.147	-0.887	–	-0.397
18	4	0.77	0.82	1.436	-0.487	–	0.925	–	-0.731	0.195	–
19	4	0.77	0.80	1.934	–	–	1.008	–	-0.808	0.084	-0.334
20	5	0.77	0.81	1.861	-0.398	–	0.965	–	-0.697	0.223	-0.218
21	5	0.77	0.79	1.907	–	0.147	1.011	–	-0.852	0.029	-0.378
22	5	0.77	0.79	1.697	–	–	1.001	0.207	-0.880	0.058	-0.376
23	6	0.77	0.79	1.748	–	0.121	1.006	0.142	-0.894	0.021	-0.399
24	2	0.76	0.79	1.225	–	–	0.957	–	-0.928	–	–
25	3	0.76	0.81	1.570	-0.371	–	0.930	–	-0.649	–	–
26	3	0.76	0.79	1.233	–	-0.006	0.957	–	-0.924	–	–
27	3	0.76	0.79	1.328	–	–	0.960	-0.058	-0.894	–	–
28	4	0.76	0.79	1.332	–	0.015	0.960	-0.072	-0.898	–	–
29	3	0.76	0.79	1.249	–	–	0.956	–	-0.912	-0.019	–
30	4	0.76	0.79	1.244	–	0.006	0.956	–	-0.914	-0.022	–
31	4	0.76	0.79	1.328	–	–	0.959	-0.052	-0.890	-0.009	–
32	5	0.76	0.79	1.333	–	0.022	0.960	-0.067	-0.893	-0.016	–
33	3	0.75	0.80	0.744	-0.544	–	0.820	–	–	–	-0.282
34	4	0.75	0.78	0.536	-0.717	0.252	0.784	–	–	–	-0.333
35	4	0.75	0.80	0.324	-0.670	–	0.780	0.260	–	–	-0.313
36	5	0.75	0.78	0.241	-0.798	0.236	0.757	0.189	–	–	-0.353
37	5	0.75	0.75	2.890	-1.124	0.436	–	1.167	-0.723	–	-0.254
38	4	0.75	0.80	0.701	-0.567	–	0.818	–	–	0.033	-0.288
39	5	0.75	0.78	0.571	-0.702	0.266	0.785	–	–	-0.036	-0.330
40	5	0.75	0.80	0.308	-0.680	–	0.779	0.254	–	0.019	-0.316
41	6	0.75	0.78	0.271	-0.784	0.253	0.757	0.198	–	-0.043	-0.349

42	6	0.75	0.76	2.851	-1.176	0.395	–	1.177	-0.767	0.134	-0.266
43	2	0.74	0.80	0.043	-0.713	–	0.751	–	–	–	–
44	3	0.74	0.79	-0.169	-0.843	0.160	0.721	–	–	–	–
45	3	0.74	0.80	-0.101	-0.755	–	0.738	0.076	–	–	–
46	4	0.74	0.79	-0.190	-0.848	0.159	0.719	0.011	–	–	–
47	4	0.74	0.75	2.528	-1.146	0.378	–	1.036	-0.741	–	–
48	4	0.74	0.77	1.234	–	-0.009	0.883	-0.489	–	–	-0.407
49	3	0.74	0.80	0.070	-0.701	–	0.753	–	–	-0.015	–
50	4	0.74	0.78	-0.082	-0.811	0.189	0.723	–	–	-0.068	–
51	4	0.74	0.80	-0.079	-0.742	–	0.738	0.084	–	-0.021	–
52	5	0.74	0.78	-0.130	-0.824	0.187	0.719	0.028	–	-0.069	–
53	5	0.74	0.76	2.481	-1.189	0.342	–	1.038	-0.778	0.110	–
54	4	0.74	0.77	1.245	–	–	0.878	-0.387	–	-0.120	-0.382
55	5	0.74	0.77	1.272	–	0.059	0.877	-0.424	–	-0.139	-0.392
56	3	0.73	0.77	1.238	–	–	0.883	-0.498	–	–	-0.409
57	4	0.73	0.80	3.012	-0.891	–	–	1.247	-0.638	–	-0.182
58	5	0.73	0.80	2.927	-1.011	–	–	1.251	-0.721	0.217	-0.212
59	3	0.72	0.73	4.212	-0.733	0.451	–	–	-0.493	–	–
60	3	0.72	0.80	2.728	-0.930	–	–	1.141	-0.660	–	–
61	3	0.72	0.77	0.438	–	-0.175	0.826	–	–	–	-0.505
62	4	0.72	0.73	4.547	-0.690	0.489	–	–	-0.466	–	-0.144
63	3	0.72	0.76	0.855	–	–	0.835	-0.659	–	-0.188	–
64	4	0.72	0.77	0.847	–	-0.031	0.836	-0.636	–	-0.177	–
65	4	0.72	0.74	4.171	-0.772	0.418	–	–	-0.527	0.104	–
66	4	0.72	0.80	2.614	-1.040	–	–	1.128	-0.735	0.188	–
67	3	0.72	0.76	0.608	–	–	0.823	–	–	-0.217	-0.482
68	4	0.72	0.77	0.637	–	-0.049	0.828	–	–	-0.194	-0.466
69	5	0.72	0.74	4.526	-0.731	0.455	–	–	-0.504	0.117	-0.154
70	2	0.71	0.76	0.786	–	–	0.840	-0.871	–	–	–
71	3	0.71	0.78	0.770	–	-0.122	0.844	-0.733	–	–	–
72	2	0.71	0.74	0.162	–	–	0.799	–	–	–	–

											0.616
73	4	0.71	0.74	2.134	-1.028	0.310	–	0.571	–	–	-0.286
74	5	0.71	0.74	2.164	-1.014	0.327	–	0.580	–	-0.044	-0.282
75	3	0.70	0.75	1.725	-1.054	0.242	–	0.404	–	–	–
76	2	0.70	0.80	4.710	-0.417	–	–	–	-0.372	–	–
77	3	0.70	0.73	3.283	-0.791	0.371	–	–	–	–	-0.214
78	3	0.70	0.79	2.309	-0.868	–	–	0.682	–	–	-0.231
79	3	0.70	0.80	4.842	-0.393	–	–	–	-0.360	–	-0.050
80	4	0.70	0.75	1.785	-1.031	0.269	–	0.421	–	-0.069	–
81	3	0.70	0.80	4.558	-0.539	–	–	–	-0.455	0.200	–
82	4	0.70	0.73	3.305	-0.783	0.378	–	–	–	-0.020	-0.211
83	4	0.70	0.79	2.279	-0.886	–	–	0.671	–	0.034	-0.237
84	4	0.70	0.81	4.759	-0.506	–	–	–	-0.440	0.211	-0.079
85	1	0.69	0.79	3.324	-0.616	–	–	–	–	–	–
86	2	0.69	0.74	2.681	-0.868	0.301	–	–	–	–	–
87	2	0.69	0.79	1.931	-0.919	–	–	0.520	–	–	–
88	2	0.69	0.79	3.768	-0.536	–	–	–	–	–	-0.126
89	2	0.69	0.79	3.214	-0.654	–	–	–	–	0.047	–
90	3	0.69	0.73	2.748	-0.847	0.321	–	–	–	-0.046	–
91	2	0.69	0.73	-0.674	–	–	0.701	–	–	-0.435	–
92	3	0.69	0.76	-0.326	–	-0.240	0.745	–	–	-0.281	–
93	3	0.69	0.79	1.931	-0.919	–	–	0.520	–	0.000	–
94	3	0.69	0.80	3.648	-0.587	–	–	–	–	0.075	-0.143
95	2	0.68	0.75	-0.764	–	-0.455	0.736	–	–	–	–
96	2	0.68	0.78	4.977	–	–	–	–	-0.524	–	-0.223
97	3	0.68	0.76	4.939	–	0.113	–	–	-0.579	–	-0.275
98	3	0.68	0.77	4.670	–	–	–	0.238	-0.620	–	-0.289
99	4	0.68	0.76	4.716	–	0.067	–	0.185	-0.631	–	-0.304
100	3	0.68	0.78	4.975	–	–	–	–	-0.531	0.012	-0.228

101	4	0.68	0.76	4.941	–	0.134	–	–	-0.564	-0.042	-0.268
102	4	0.68	0.77	4.655	–	–	–	0.255	-0.610	-0.028	-0.283
103	5	0.68	0.76	4.702	–	0.091	–	0.200	-0.615	-0.055	-0.299
104	1	0.67	0.76	4.311	–	–	–	–	-0.659	–	–
105	2	0.67	0.77	4.327	–	-0.010	–	–	-0.652	–	–
106	2	0.67	0.76	4.314	–	–	–	-0.001	-0.658	–	–
107	3	0.67	0.77	4.309	–	-0.014	–	0.012	-0.656	–	–
108	2	0.67	0.77	4.391	–	–	–	–	-0.607	-0.062	–
109	3	0.67	0.76	4.356	–	0.035	–	–	-0.619	-0.079	–
110	3	0.67	0.76	4.292	–	–	–	0.056	-0.629	-0.074	–
111	4	0.67	0.76	4.299	–	0.024	–	0.038	-0.630	-0.082	–
112	3	0.65	0.74	3.919	–	–	–	-0.142	–	-0.152	-0.303
113	2	0.64	0.74	3.402	–	-0.105	–	–	–	–	-0.397
114	2	0.64	0.75	3.927	–	–	–	-0.277	–	–	-0.340
115	3	0.64	0.75	3.922	–	-0.010	–	-0.268	–	–	-0.337
116	2	0.64	0.73	3.528	–	–	–	-0.373	–	-0.206	–
117	3	0.64	0.73	3.528	–	–	–	-0.373	–	-0.206	–
118	2	0.64	0.73	3.628	–	–	–	–	–	-0.189	-0.345
119	3	0.64	0.73	3.610	–	0.020	–	–	–	-0.199	-0.352
120	4	0.64	0.73	3.951	–	0.071	–	-0.188	–	-0.174	-0.316
121	1	0.63	0.75	3.466	–	–	–	-0.603	–	–	–
122	2	0.63	0.78	3.457	–	-0.104	–	-0.482	–	–	–
123	1	0.63	0.71	3.191	–	–	–	–	–	–	-0.468
124	2	0.63	0.74	2.657	–	-0.133	–	–	–	-0.269	–
125	1	0.62	0.69	2.363	–	–	–	–	–	-0.357	–
126	1	0.61	0.73	2.197	–	-0.338	–	–	–	–	–
127	1	0.61	0.64	-2.973	–	–	0.561	–	–	–	–

Blind sample test set: Quantitative RT-PCR analysis of gene expression in an independent blind test set of blood samples from 76 subjects having colorectal cancer and 77 subjects not having any colorectal pathology was performed as described above for the training set. The normalized RNA levels measured are shown in Table 7.

Table 7. Sample test set levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by ACTB. Levels shown correspond to ΔCt.

Sample ID	Group	Gene						
		ANXA3	CLEC4D	IL2RB	LMNB1	PRRG4	TNFAIP6	VNN1
CD0214pax	0	5.56	6.17	4.50	6.44	7.07	5.78	6.69
CD0242pax	0	5.87	7.32	4.54	5.43	5.19	5.87	7.38
RC2897pax	0	6.67	8.37	5.49	5.95	7.18	7.80	7.96
CD0670pax	0	7.79	5.80	3.25	6.35	7.10	8.40	7.80
CD1401pax	0	5.84	6.39	5.42	5.85	7.30	6.55	7.12
PB2924pax	0	5.56	7.17	4.12	5.97	6.51	5.90	7.12
CD0482pax	0	7.65	8.34	3.43	6.91	7.02	8.94	8.48
PB1275pax	0	5.26	6.13	5.18	5.54	7.09	5.89	8.78
CD0148pax	0	5.90	7.83	3.98	5.95	7.60	7.35	7.20
CD0122pax	0	6.55	8.40	5.02	6.38	7.07	7.96	8.83
PB2272pax	0	7.30	8.30	3.95	6.57	7.42	9.42	7.49
CD1708pax	0	6.28	9.11	4.07	5.74	6.01	7.48	7.13
CD0354pax	0	6.55	8.20	4.93	6.30	8.06	8.28	7.81
PB2634pax	0	5.76	7.74	5.28	6.80	7.20	9.18	7.39
CD0204pax	0	5.90	6.53	4.83	5.56	6.25	7.29	6.87
PB1336pax	0	7.60	9.00	6.87	6.99	7.13	8.92	9.71
RC2699pax	0	7.72	9.42	6.03	7.12	7.99	8.67	8.57
CD1278pax	0	5.95	7.57	4.20	5.72	6.31	6.83	7.36
PB2062pax	0	7.31	7.76	4.31	6.50	7.29	8.38	7.78
PB2464pax	0	5.95	8.33	4.73	5.52	5.52	6.39	8.43
CD0053pax	0	6.17	7.90	4.09	6.56	7.18	8.25	7.44
CD0192pax	0	5.49	7.60	4.19	5.66	7.38	5.48	6.03
CD0244pax	0	6.32	7.31	5.26	6.21	7.56	7.63	6.89
CD0833pax	0	5.52	8.65	4.72	5.55	6.33	6.60	5.47
CD1719pax	0	6.19	7.94	5.40	5.93	6.39	6.50	7.51
CD0036pax	0	5.20	5.95	4.60	4.95	4.51	5.99	5.82
PB2015pax	0	6.62	7.13	3.85	5.99	7.62	8.53	7.13
PB0662pax	0	6.09	7.17	5.33	6.49	7.40	7.43	6.60
PB2024pax	0	6.16	6.10	4.49	5.94	6.86	8.23	7.44
RC2565pax	0	6.63	8.81	5.94	6.33	8.38	7.11	8.75
CD1561pax	0	7.29	6.78	4.73	6.48	7.49	8.18	8.21
CD1728pax	0	7.13	6.89	4.30	6.52	7.76	7.08	8.63
CD0238pax	0	5.47	7.06	4.85	6.10	7.13	7.38	7.14

PB2342pax	0		7.65	4.19	6.21	7.29	8.02	8.00
CD0800pax	0	7.42	8.19	3.99	6.61	7.78	8.79	8.44
CD0437pax	0	4.74	5.92	5.05	4.90	5.58	6.27	6.17
RC3214pax	0	6.35	8.13	4.96	6.22	7.02	8.19	7.01
CD1487pax	0	5.24	7.83	4.51	5.99	7.26	7.36	6.48
PB1763pax	0	7.83	9.12	5.21	7.40	8.78	9.20	8.37
CD0580pax	0	5.14	5.72	3.17	4.54	4.78	6.28	5.28
CD0840pax	0	4.94	6.63	4.96	5.38	5.60	6.63	6.10
PB2757pax	0	5.32	7.54	4.98	5.51	6.48	6.77	8.12
PB2184pax	0	5.11	7.34	5.73	5.68	6.63	6.30	8.26
PB2179pax	0	5.57	6.84	4.80	5.59	5.75	5.74	6.56
PB1324pax	0	4.77	9.26	4.24	5.57	6.78	7.16	7.37
CD0237pax	0	6.46	8.06	5.42	5.89	6.89	7.51	7.26
CD1329pax	0	6.03	6.72	4.93	5.93	6.06	7.37	7.38
PB2005pax	0	7.51	7.37	4.66	6.41	7.63	9.46	8.15
PB3227pax	0	5.08	6.46	4.44	5.74	6.46	7.62	7.51
PB3163pax	0	4.51	6.23	4.17	5.32	6.10	7.12	6.54
PB3481pax	0	5.66	7.99	5.16	5.95	8.33	6.48	8.26
CD1320pax	0	4.16	5.93	4.79	4.60	5.55	5.10	6.16
RC3191pax	0	7.15	7.64	4.92	6.94	7.20	8.20	8.30
CD0583pax	0	4.29	7.00	4.44	4.16	3.96	8.82	3.97
PB3032pax	0	5.12	6.51	5.09	5.96	6.08	6.91	7.87
CD0367pax	0	5.75	6.68	4.34	5.49	6.25	7.12	7.06
PB2889pax	0	6.03	8.25	4.75	6.39	7.27	7.04	7.68
PB3524pax	0	6.66	6.73	5.40	6.83	7.72	6.07	7.38
RC2986pax	0	6.90	7.96	5.36	6.14	7.22	8.87	7.75
CD1428pax	0	6.64	9.25	3.67	5.82	7.04	7.12	6.09
RC2236pax	0	6.82	6.87	5.24	6.21	7.41	7.27	8.02
PB1918pax	0	8.72	7.41	5.20	7.28	8.29	10.44	9.02
CD0277pax	0	6.42	8.60	5.37	6.63	7.61	8.57	7.04
CD0667pax	0	5.15	6.09	5.57	5.26	6.33	6.27	6.41
CD1741pax	0	5.46	6.18	5.57	5.76	6.50	7.24	7.18
PB1973pax	0	8.07	9.15	4.68	7.12	8.89	9.13	10.01
PB1222pax	0	5.80	7.45	5.57	5.95	5.81	6.15	7.61
RC2683pax	0	8.25	9.29	5.83	6.98	8.07	9.46	9.66
PB3200pax	0	5.00	6.73	4.23	5.42	6.59	6.31	7.35
PB2130pax	0	6.31	7.61	4.91	5.50	5.79	6.48	6.81
PB3097pax	0	6.33	3.94	5.77	6.08	6.72	7.78	7.51
CD0571pax	0	5.28	6.04	3.76	5.54	6.60	6.99	5.82
CD0676pax	0	5.50	6.68	5.78	5.79	5.91	6.91	7.18
PB1514pax	0	7.57	5.96	5.35	7.38	8.09	7.63	8.37
CD0547pax	0	4.62	7.13	6.05	5.85	7.44	6.70	6.88
CD1068pax	0	5.79	6.49	4.84	6.23	7.14	8.55	6.32
CD0715pax	0	2.97	4.03	4.74	4.51	4.94	5.38	6.46
JH0130pax	1	5.32	5.90	6.01	5.47	5.77	5.93	6.90
MH0079pax	1	6.41	6.17	5.06	6.19	6.42	6.61	7.57

MH0082pax	1	7.06	4.93	5.26	6.82	6.74	8.27	7.32
AN0013pax	1	4.94	7.96	3.89	5.60	5.49	7.86	7.95
NK2005pax	1	4.20	5.83	5.59	5.08	5.65	4.02	6.98
CD1111pax	1	6.62	6.64	4.17	6.17	7.32	7.62	7.72
JH0105pax	1	5.31	7.29	4.84	5.39	5.34	7.13	8.28
MIP1007pax	1	3.42	7.30	4.89	4.27	6.00	5.13	3.62
DC0011pax	1	4.33	5.63	4.17	5.45	5.74	6.41	7.06
MH0073pax	1	4.68	6.28	5.84	4.57	5.52	6.41	5.86
DC0003pax	1	6.24	7.65	5.02	6.05	6.64	7.05	8.46
DC1002pax	1	4.62	4.35	5.41	5.26	6.40	7.24	6.90
JH0096pax	1	3.45	5.49	5.18	4.79	5.74	3.34	7.61
KW0002pax	1	4.26	6.89	4.62	4.71	4.76	5.78	6.53
JH0120pax	1	5.89	4.91	5.53	6.38	5.56	8.45	6.44
MIP1008pax	1	4.84	7.74	5.47	5.41	5.63	5.36	6.93
MIP0002pax	1	3.76	6.96	5.63	4.85	6.55	5.74	6.87
MIP1011pax	1	4.70	6.28	5.12	4.63	4.60	5.68	4.55
MH0074pax	1	5.11	5.73	5.75	5.68	6.74	7.59	6.00
DC0008pax	1	4.97	6.33	4.16	5.44	4.95	6.54	5.87
AN4014pax	1	3.93	5.76	4.25	4.58	5.76	5.20	7.74
DC0012pax	1	4.25	6.07	5.15	5.08	7.00	4.86	6.37
MIP2002pax	1	5.54	5.71	4.26	5.54	5.77	6.57	6.33
NK1005pax	1	5.76	8.79	5.22	7.02	7.38	8.60	7.55
MIP0007pax	1	2.91	3.55	6.69	3.21	4.38	3.48	4.85
JH0118pax	1	5.72	7.53	4.77	5.56	5.85	6.56	6.04
JH0089pax	1	5.11	7.30	4.99	5.68	5.58	6.54	7.38
MH0057pax	1	5.80	6.60	6.01	6.35	6.36	7.44	6.44
DC0005pax	1	5.98	7.66	4.72	6.38	6.39	7.47	7.19
MH0067pax	1	4.75	6.06	6.11	4.96	5.30	6.78	5.54
JH0085pax	1	5.19	6.48	5.92	5.99	5.76	6.65	7.12
JH0127pax	1	5.48	6.43	5.18	6.13	7.59	6.63	7.04
MIP1013pax	1	4.86	5.89	4.56	5.29	5.21	5.89	6.51
JH0126pax	1	4.21	7.08	5.35	5.68	5.40	5.50	7.07
AN4013pax	1	5.15	5.66	4.15	5.19	5.38	5.94	6.91
MH0053pax	1	7.07	8.10	4.16	6.42	5.83	8.33	7.84
JH0115pax	1	3.82	7.54	5.74	4.75	6.03	6.27	7.36
CC0004pax	1	3.83	5.81	4.59	4.67	5.46	5.50	5.84
JH0091pax	1	5.26	5.92	4.74	5.31	7.34	6.70	6.91
NK1004pax	1	5.76	7.32	6.16	5.78	6.58	7.99	7.77
NK1008pax	1	4.70	7.52	5.56	5.57	6.80	6.58	7.52
MIP2006pax	1	4.25	6.38	4.28	4.74	5.69	5.36	5.38
AN0020pax	1	4.12	6.61	5.57	4.81	4.61	4.45	6.07
JH0117pax	1	3.36	8.59	4.90	4.29	4.99	5.12	5.76
JH0100pax	1	5.54	6.69	4.86	5.66	6.57	7.23	7.26
MH0066pax	1	5.12	5.25	6.28	5.59	6.61	6.27	6.13
NK2009pax	1	5.30	5.93	4.95	5.76	5.27	7.71	5.77
NK2008pax	1	4.14	5.57	5.88	4.93	5.45	6.59	5.66

PB3067-2pax	1	5.84	8.25	4.70	6.20	6.51	7.78	6.81
NK1003pax	1	4.41	6.99	5.48	5.30	6.08	6.48	7.13
MIP1009pax	1	3.22	8.02	6.45	4.25	5.14	5.47	5.21
DC2006pax	1	6.06	5.91	4.81	5.88	6.05	7.24	7.34
JH0131pax	1	5.19	6.71	4.98	5.21	5.15	4.75	6.43
DC0015pax	1	4.95	6.98	5.01	5.46	6.53	6.02	6.17
AN0001pax	1	4.36	6.54	5.97	5.60	5.83	6.72	7.13
JH0111pax	1	5.04	6.83	4.22	5.09	6.96	7.14	5.78
MIP0005pax	1	3.74	5.56	5.98	4.46	5.80	5.74	5.33
MH0065pax	1	4.50	5.37	5.63	5.51	6.30	6.09	5.82
JH0136pax	1	3.39	4.63	6.12	4.86	5.19	7.76	4.59
CD1351pax	1	6.86	7.94	5.55	6.06	6.52	8.46	7.62
MH0075pax	1	6.05	7.17	5.57	5.77	6.75	7.32	7.27
MH0078pax	1	4.60	6.70	5.49	5.26	4.21	5.25	7.54
MH0068pax	1	7.58	5.49	4.48	6.43	7.14	8.00	6.36
MIP2003pax	1	4.24	5.60	4.30	4.93	6.05	6.85	5.97
NK2015pax	1	5.42	5.52	5.54	6.08	6.40	8.40	8.09
MH0070pax	1	5.40	7.11	4.66	5.74	6.55	7.09	7.08
JH0093pax	1	5.22	7.62	4.66	5.29	5.39	7.00	7.15
JH0135pax	1	4.40	4.64	5.52	4.62	5.38	4.31	4.62
CD1571pax	1	5.45	6.48	4.41	5.65	7.26	7.88	7.17
MH0061pax	1	4.99	5.15	5.47	5.72	6.73	7.65	7.76
NK2007pax	1	5.98	7.25	5.17	5.76	7.02	7.32	6.38
JH0132pax	1	5.29	7.18	5.29	5.76	6.96	6.66	6.83
MH0062pax	1	4.40	6.01	4.86	5.42	5.50	6.26	6.45
JH0114pax	1	4.78	6.93	7.12	5.58	7.50	5.62	5.26
CD1260pax	1	5.28	5.92	5.24	5.73	5.86	7.18	7.37
JH0022pax	1	5.00	5.94	4.73	5.49	6.17	5.66	6.80

Analysis of the test set results confirmed the surprising finding based on the training set that ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 each express RNA on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology, and that IL2RB expresses RNA on average at a significantly lower level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 8). The ranges of fold-change in the levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by ACTB in blood of the test set subjects having colorectal cancer relative to the test set subjects not having any colorectal pathology are also shown in Table 8.

Table 8. Sample test set ranges of fold-change in levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6, VNN1 normalized to levels of RNA encoded by ACTB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene						
	ANXA3	**CLEC4D**	**IL2RB**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**
Average normalized RNA level in subjects having colorectal cancer (ΔCt)	4.98	6.45	5.18	5.42	6.01	6.51	6.63
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	6.10	7.32	4.83	6.01	6.86	7.41	7.40
Average RNA level fold-change	2.17	1.82	0.78	1.50	1.80	1.87	1.70
p-value for average RNA level fold-change	1.7E-10	1.9E-06	1.4E-03	1.3E-07	1.6E-08	3.8E-06	4.4E-06
Maximum observed RNA level directional fold-change	9.13	13.66	0.20	6.98	6.26	16.78	13.78

As can be seen in Table 8, a test subject having a blood level of RNA encoded by ANXA3 which is 2.2 to 9.1 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by CLEC4D which is 1.8 to 13.7 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by LMNB1 which is 1.5 to 7.0 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by PRRG4 which is 1.8 to 6.3 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by TNFAIP6 which is 1.9 to 16.8 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by VNN1 which is 1.7 to 13.8 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 8, a test subject having a blood level of RNA encoded by IL2RB which is 0.8 to 0.2 fold that of the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Furthermore, the test set results confirmed the surprising finding based on the training set that logistic regression models based on blood expression levels for any of the 127 possible combinations of one or more of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, each of which normalized against expression levels of ACTB, can be used to discriminate, with a ROC AUC of at least 0.64 (Table 6), between subjects having colorectal cancer and subjects not having any colorectal pathology. As such, the novel logistic regression models listed in Table 6 can be used to determine the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, based on blood levels of expression of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and/or VNN1.

EXAMPLE 3

Measurement of blood levels of RNA encoded by any combination of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and/or VNN1 relative to the level of RNA encoded by IL2RB can be used to determine the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology

MATERIALS AND METHODS:

Refer to "General materials and methods", above.

EXPERIMENTAL RESULTS:

Sample training set:

Discovery of significantly different levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, VNN1, TNFAIP6 normalized to IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology: Quantitative reverse transcriptase-PCR analysis of gene expression in a training set of blood samples from 116 subjects having colorectal cancer and 127 subjects not having any colorectal pathology, using IL2RB as duplex partner for normalization of gene expression levels was performed. The normalized RNA levels measured are shown in Table 9

Table 9. Sample training set levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by IL2RB. Levels shown correspond to ΔCt.

Sample ID	**Group**	**Gene**					
		ANXA3	**CLEC4D**	**LMNB1**	**PRRG4**	**TNFAIP 6**	**VNN1**
CD0011pax	0	0.8303	1.3467	1.2008	0.8909	2.1665	2.6036
CD0012pax	0	1.2503	1.4917	0.8258	0.9309	1.9115	2.9086
CD0030pax	0	1.2878	1.2957	0.7182	1.1632	0.7535	1.7757
CD0063pax	0	2.4078	3.0807	1.6332	1.8532	3.4685	3.0157
CD0077pax	0	-0.0047	1.2417	0.7058	0.7009	0.8465	1.7436
CD0078pax	0	1.6928	2.4057	0.9432	0.9332	2.6735	1.4807
CD0085pax	0	0.4428	1.5007	0.4032	0.8232	2.4335	0.4457
CD0117pax	0	0.6028	2.2057	0.7632	2.0182	2.2585	0.6557
CD0146pax	0	0.0353	0.7117	0.6708	0.1659	1.3215	0.7236
CD0167pax	0	-1.3147	-0.1483	0.0358	0.2609	1.3315	0.0786
CD0249pax	0	-0.7797	-0.6233	-0.8142	0.0609	-0.0085	0.2486
CD0279pax	0	0.8278	1.9907	0.7632	0.7382	1.6185	1.4957
CD0286pax	0	0.0753	1.5217	0.7058	0.6659	0.7215	0.7286
CD0297pax	0	-0.1797	0.2867	0.1958	-0.3291	0.0665	0.4836
CD0323pax	0	1.7303	1.6817	0.5408	1.2359	2.2865	3.0636
CD0445pax	0	0.9878	1.2107	0.6682	0.6932	1.8085	1.6907
CD0463pax	0	-0.3647	1.2267	0.3058	0.5559	1.2365	1.0136

CD0491pax	0	-0.3972	0.3507	0.4482	0.7032	1.1785	0.2907
CD0496pax	0	0.8753	2.4167	0.6958	1.4509	1.0515	0.6436
CD0501pax	0	0.8753	1.7517	0.9558	0.9109	2.7615	1.0986
CD0504pax	0	-0.4947	0.2367	0.2358	1.0209	0.3715	0.7936
CD0573pax	0	1.9978	1.3107	0.9582	0.9982	2.4435	1.9357
CD0578pax	0	1.6103	1.7317	0.6408	0.6259	1.6865	1.7136
CD0639pax	0	0.1028	0.6657	0.6232	-0.2618	0.9985	1.5857
CD0645pax	0	-0.8347	-0.1883	-0.4342	-0.4441	0.4965	0.0986
CD0679pax	0	0.4703	1.7767	0.6658	0.5659	1.9465	2.2636
CD0685pax	0	0.8753	2.3317	0.8008	1.3759	2.1915	1.4836
CD0716pax	0	1.9978	2.4057	0.9182	0.4432	1.5835	2.0457
CD0749pax	0	0.3303	1.3717	0.4058	0.5509	2.0465	1.0336
CD0760pax	0	-2.5747	-1.3583	-1.9442	-1.1491	-1.2335	-0.8714
CD0811pax	0	2.2353	2.8417	1.1858	1.3609	1.3865	1.3286
CD0846pax	0	-0.6522	0.3407	-0.6418	-0.3468	-0.6315	1.5657
CD0848pax	0	0.7278	1.2057	0.9832	1.0232	1.5785	1.8307
CD0924pax	0	0.1428	0.5357	-0.0768	-0.4418	0.2935	-0.0793
CD1066pax	0	0.1753	0.6667	0.2658	0.2059	1.9715	0.5786
CD1073pax	0	0.1053	-0.0633	-0.0092	-0.1341	0.8015	1.0886
CD1075pax	0	-0.3322	0.4757	-0.0118	1.1582	1.2385	0.1957
CD1089pax	0	-1.1072	0.1657	-0.7818	-0.5318	0.1935	-0.1193
CD1116pax	0	-0.2072	-0.0543	-0.2818	0.2982	1.4885	0.4107
CD1120pax	0	-0.8872	0.0357	-0.5868	0.2032	1.1885	-0.2443
CD1198pax	0	0.5253	0.5317	0.7908	0.7509	0.7915	0.9786
PB1179pax	0	1.0003	1.0617	0.8808	0.9909	2.4315	1.2286
PB1277pax	0	0.8803	1.4817	0.4258	0.9859	1.5765	0.8286
PB1301pax	0	-1.7247	-0.9183	-0.9092	-0.5091	-0.6985	-1.2864
PB1315pax	0	-1.5572	0.2257	-0.6218	-0.3118	-0.2015	0.9007
PB1345pax	0	0.1953	0.6617	0.7508	1.0459	0.3615	2.0236
PB1518pax	0	1.2653	1.6967	0.2058	0.8359	1.3565	1.3036
PB1520pax	0	1.0953	2.0267	0.9708	0.0109	1.6565	2.2236
PB1574pax	0	1.0753	1.5467	0.8008	0.6109	1.0465	1.1836
PB1783pax	0	1.5978	1.7007	1.1982	1.2632	2.1135	1.5907
PB1799pax	0	0.6978	1.0157	0.5282	1.0632	2.0785	0.5957
PB1811pax	0	0.8628	1.4057	0.8232	1.2632	1.3685	0.9507
PB1830pax	0	0.1428	0.6807	0.2532	0.1182	0.8985	2.3407
PB1833pax	0	0.2028	1.1407	0.4782	0.5532	0.9385	1.5457
PB1843pax	0	0.5553	0.4717	0.0708	0.5909	-0.5285	1.1486
PB1851pax	0	0.4428	0.1007	0.2632	0.3232	2.7035	1.6007
PB1919pax	0	1.4703	2.1067	0.8108	1.7959	2.1365	2.5086
PB1922pax	0	0.3103	1.1867	0.4258	1.3759	2.1215	0.9986
PB1924pax	0	0.2428	0.5357	0.1632	0.3632	1.1535	1.2357
PB1937pax	0	1.3128	2.1057	1.0982	2.9132	2.4835	2.2007
PB1964pax	0	0.4828	2.6207	0.7382	1.5332	2.4035	2.7507
PB2027pax	0	-0.1422	0.3857	0.1582	0.3182	1.1835	1.5807
PB2029pax	0	0.1953	0.5917	0.0708	-0.0391	1.8615	0.7336

PB2073pax	0	0.4478	0.9057	0.4382	1.6632	1.5085	0.9257
PB2086pax	0	0.1153	0.1817	0.3108	0.8409	0.3215	0.5386
PB2099pax	0	-0.4622	-0.5993	-0.1568	0.0732	-0.1265	0.1057
PB2100pax	0	1.1628	1.1057	0.6532	1.5482	2.1385	1.1507
PB2132pax	0	0.5503	1.1517	0.3558	0.6109	2.1315	1.4536
PB2168pax	0	1.3278	1.5357	0.8482	1.1682	2.3435	1.3307
PB2192pax	0	0.3153	0.8967	0.3308	-0.0291	1.2515	1.9286
PB2196pax	0	0.8328	1.6107	0.7932	1.4432	2.0535	1.2107
PB2200pax	0	1.1028	1.4807	0.3732	0.4432	0.9635	0.5757
PB2213pax	0	2.1753	2.2717	1.1658	0.9009	3.1465	1.9736
PB2224pax	0	-0.2772	0.6207	0.0482	0.3582	2.1235	1.2607
PB2228pax	0	1.7703	2.1017	1.3658	1.6859	3.6965	2.7186
PB2229pax	0	-0.2047	-0.3183	-0.0542	-0.9241	0.5615	-0.1764
PB2277pax	0	1.3578	0.8507	0.6332	0.3582	1.0785	1.7457
PB2297pax	0	0.4178	1.1507	0.1282	0.0332	0.9235	-0.3343
PB2312pax	0	1.3628	2.0057	1.4132	0.9632	2.0885	2.0357
PB2398pax	0	-0.5822	0.1007	-0.2868	-0.7518	-0.1865	1.3307
PB2409pax	0	0.1153	0.6817	0.3008	0.3359	1.0115	1.5036
PB2414pax	0	2.7128	2.3707	1.2132	2.1832	3.6985	1.9707
PB2467pax	0	0.7478	1.1457	0.5482	0.6382	2.2385	1.3607
PB2473pax	0	0.3828	0.8857	0.4432	1.0932	0.9185	1.8407
PB2512pax	0	0.7003	1.7267	0.8458	0.4709	1.8115	2.0136
PB2568pax	0	-0.4772	0.0157	-0.3718	0.4132	1.2435	1.0857
PB2571pax	0	0.3003	1.0017	0.5558	0.2609	1.8915	1.9336
PB2603pax	0	1.0128	1.4757	1.1082	1.1632	2.3335	0.7457
PB2624pax	0	0.4403	0.5167	0.7208	1.3259	1.3865	1.2286
PB2824pax	0	0.5178	0.9907	0.4582	1.0132	1.8135	1.3207
PB2880pax	0	1.0403	1.0617	0.6208	-0.2491	1.8615	1.5586
PB3088pax	0	1.6503	1.7517	1.3208	1.1359	3.4165	2.3786
RC0882pax	0	0.2728	1.4507	0.6582	0.7682	2.0985	1.8007
RC0888pax	0	-0.7872	-0.3193	-0.2118	0.2932	0.7835	0.2957
RC0968pax	0	-0.8522	-0.6493	0.0182	1.4382	0.7835	2.1457
RC2114pax	0	-0.4722	0.7557	0.0282	0.4132	0.1335	1.9357
RC2238pax	0	0.9528	1.8557	0.5982	1.5182	2.4435	2.8857
RC2681pax	0	0.3278	1.1957	0.4582	0.5532	0.7435	0.9507
RC2703pax	0	1.6403	1.8317	0.7658	1.1959	1.1615	1.1436
RC2749pax	0	0.3978	1.1407	0.3632	0.4682	1.6635	1.5157
RC2750pax	0	-1.7872	-1.2393	-1.0418	-0.3118	-0.1115	-0.6943
RC2756pax	0	1.3803	0.9167	0.5508	1.0009	1.6415	1.9636
RC2771pax	0	-0.9547	0.3567	-0.6792	-0.3341	1.1965	1.4536
RC2790pax	0	0.8953	0.9817	0.4808	0.7259	1.0815	1.3536
RC2792pax	0	1.2903	0.8667	0.8058	1.4559	1.9415	1.5836
RC2808pax	0	0.7953	1.9117	0.7558	1.0009	1.1715	1.4036
RC2822pax	0	0.7728	1.2607	0.3282	0.5932	2.5785	0.5807
RC2834pax	0	-0.6247	0.2917	-0.5742	0.9309	2.0765	0.9236
RC2871pax	0	0.9028	1.4107	1.1032	1.5332	2.6485	2.6307

RC2879pax	0	-0.2047	0.3867	-0.0342	0.8509	0.6315	0.5086
RC2892pax	0	-0.0022	0.5557	-0.0968	0.7032	2.0385	1.1857
RC2895pax	0	1.7178	1.9857	1.2632	1.3682	1.4435	2.0557
RC2921pax	0	1.3153	1.2967	1.0058	1.3709	2.0315	2.0886
RC2958pax	0	1.0553	1.1017	0.4958	0.1409	0.4965	1.4836
RC3022pax	0	0.3028	0.3007	0.3582	1.0432	1.7635	0.4707
RC3112pax	0	1.2553	1.4667	0.5908	0.5759	2.5515	1.3286
RC3146pax	0	-0.1572	-0.2793	-0.4918	0.1432	1.0235	0.8307
RC3184pax	0	2.1353	2.5967	1.0758	1.3559	2.2865	2.2336
RC3232pax	0	-0.3747	0.5667	-0.5942	0.5309	-0.4385	2.3786
RC3324pax	0	0.2128	0.8557	0.0082	0.3282	1.3985	-0.0693
RC3327pax	0	0.2003	-0.1333	-0.0292	-0.2491	1.2315	1.8086
RC3355pax	0	0.0328	0.5657	-0.2668	-0.0418	1.2935	0.4857
RC3380pax	0	-0.4372	0.4907	-0.3518	-0.0318	0.5235	0.0757
RC3413pax	0	0.6028	1.1907	0.4532	0.0182	0.8435	2.3907
RC3421pax	0	-0.0047	0.2917	-0.0142	0.1409	-0.0735	-0.0964
RC3468pax	0	-0.1022	-0.0143	-0.0618	-0.3368	1.1485	0.2907
RC3498pax	0	0.0353	-0.2633	-0.1892	0.2909	1.2415	0.2486
CC0003pax	1	-1.4122	-0.3593	-0.9318	-0.6468	0.8435	-0.8893
CD0157pax	1	1.5153	1.5517	1.1308	1.3209	3.0715	2.8186
CD0164pax	1	-0.0247	0.4667	0.6758	1.0059	2.5315	1.2886
CD0256pax	1	-0.6322	0.0807	0.0032	0.0382	0.8935	1.1557
CD0322pax	1	-1.1572	-0.4693	-0.8368	-0.2818	0.5435	1.0507
CD0356pax	1	-0.6772	-1.1393	-0.7718	-0.8668	-0.2215	-1.1643
CD0371pax	1	0.1028	0.9607	-0.1918	-0.3018	0.8385	-0.2843
CD0629pax	1	-0.0772	0.5407	0.5382	1.3882	0.2885	1.2507
CD1050pax	1	0.8153	0.1417	0.2208	0.7559	1.3815	1.0836
DC0001pax	1	0.1353	-0.4183	0.1208	-0.0941	0.3065	0.0936
DC0002pax	1	0.9878	0.2857	0.3632	-0.1718	1.7035	0.9057
DS0003pax	1	-1.8347	-0.7183	-1.5192	-1.5591	-0.3485	0.6886
FC0005pax	1	0.0928	0.1507	0.2682	0.1732	0.4235	1.8157
FC0011pax	1	-0.4572	-0.0793	-0.1118	-0.2318	0.8635	0.2707
FC0012pax	1	-2.5847	-0.4033	-1.3792	-1.2541	-0.2885	-0.3614
JGA0001pax	1	-2.3247	-1.6483	-1.5592	-0.7241	-1.2535	-1.1814
JGA0008pax	1	-0.6772	1.0357	0.5732	0.0932	0.8485	0.7057
JH0002pax	1	0.5453	0.9667	0.5608	0.4459	1.4065	0.7586
JH0003pax	1	0.2853	0.1667	-0.2292	-0.3941	-0.1385	1.0886
JH0004pax	1	-0.1747	-0.1733	-0.3592	-0.5591	1.1515	0.6686
JH0005pax	1	0.0928	1.2207	0.0682	0.1482	1.5735	1.1757
JH0006pax	1	-0.6397	0.0667	-0.2692	-0.2741	0.8715	-0.3114
JH0007pax	1	-2.6372	-2.2043	-1.6168	-0.5018	-0.0865	-1.2993
JH0008pax	1	0.5453	2.4167	0.2208	0.8859	2.1315	0.6336
JH0009pax	1	-0.8522	-0.7793	-0.0968	-0.6668	-0.1815	0.4507
JH0010pax	1	-0.3847	0.6517	0.2208	0.3059	0.6365	-0.2664

JH0012pax	1	-0.1072	0.3857	0.2882	0.0432	0.6685	0.9807
JH0013pax	1	-0.3022	0.2007	-0.3118	-0.0568	2.0485	0.8357
JH0014pax	1	1.1828	1.2107	0.3182	-0.0418	2.0485	2.5207
JH0016pax	1	0.5053	0.9167	0.6658	0.2659	0.4715	0.8636
JH0018pax	1	-1.1972	-0.1493	-0.4268	-0.4318	-0.1465	0.3207
JH0019pax	1	0.1153	0.6267	0.0558	-0.2091	0.1565	0.1936
JH0020pax	1	0.2728	2.0207	0.7332	-0.1518	0.7585	1.3107
JH0021pax	1	-0.8297	0.7867	-0.3992	-0.8541	0.2615	0.0586
JH0023pax	1	-0.2272	1.3307	0.5182	1.6882	1.2985	1.9507
JH0024pax	1	1.0653	2.5467	1.2508	1.4159	3.3465	2.9786
JH0025pax	1	-0.7847	-0.3833	-0.4292	-0.8891	-0.2435	0.5136
JH0026pax	1	-1.1522	0.5857	-0.0418	-0.3468	1.1035	1.1507
JH0027pax	1	-3.3947	-2.5983	-2.3842	-2.0791	-2.3435	-1.8814
JH0028pax	1	0.3253	1.0967	0.9908	0.7459	2.5415	1.4586
JH0029pax	1	-1.3522	-0.6093	-0.5918	-0.7818	-0.5615	0.5557
JH0031pax	1	-0.7297	0.2817	-0.2092	-0.2791	0.5615	0.5136
JH0032pax	1	1.5478	1.7557	0.4532	0.3732	1.7785	1.8307
JH0033pax	1	-0.8797	1.0817	-0.4242	-0.6141	1.3865	-0.1914
JH0034pax	1	-0.5397	1.0667	0.4908	0.3909	1.5465	1.5186
JH0035pax	1	-0.3222	1.3857	0.2782	-0.3268	1.9385	0.8207
JH0036pax	1	0.8128	1.0107	0.4032	0.2182	1.9235	1.1757
JH0038pax	1	0.3103	1.5367	0.2258	0.4109	2.1215	0.8386
JH0039pax	1	0.5278	0.6207	0.5032	1.1232	3.1135	0.0857
JH0040pax	1	0.4353	0.8117	0.5508	0.3259	1.2465	0.8636
JH0041pax	1	0.7303	1.7117	0.4508	0.2759	1.9565	1.0436
JH0042pax	1	-2.2922	-0.6293	-1.2268	-0.7568	-1.0515	-1.7443
JH0043pax	1	-0.8022	-0.1993	-0.2918	-0.9318	-0.3015	-0.2393
JH0046pax	1	-0.0447	0.0567	0.6408	-0.2541	0.8965	0.0336
JH0047pax	1	0.1728	1.9907	0.6082	1.2782	1.6085	2.0757
JH0051pax	1	-0.9647	-0.1533	-0.3892	-1.0491	-0.2135	-0.4064
JH0052pax	1	-0.6597	0.3067	-0.4442	-0.9141	-0.4585	-0.7914
JH0053pax	1	-0.9522	-0.1693	-0.5918	-0.0318	-0.2515	0.1107
JH0057pax	1	-0.1872	1.9757	0.1432	0.6682	1.4335	1.2057
JH0059pax	1	-0.7897	0.0717	-0.3442	-0.3241	0.3215	0.1136
JH0060pax	1	-1.0122	0.1207	-0.2818	0.0482	0.3385	0.3557
JH0061pax	1	0.7803	2.5567	0.5558	1.0309	3.2565	0.3136
JH0063pax	1	-0.2197	1.0467	0.2458	-0.4141	0.8115	2.0486
JH0065pax	1	-2.7497	-1.4333	-2.0542	-2.8691	-1.5035	-0.4814
JH0066pax	1	-1.1972	-0.0343	-0.8418	-1.6318	-1.0715	-0.4643
JH0068pax	1	0.3653	0.8867	0.7108	0.4809	1.7165	2.1986
JH0069pax	1	-0.6447	0.3967	-0.0892	-0.1791	-0.0735	-0.4014
JH0071pax	1	-2.3272	-2.1943	-1.6968	-1.0318	-1.2715	-0.3743
JH0072pax	1	-0.1197	-0.7533	-0.0892	-0.6741	1.1515	0.0586
JH0077pax	1	-0.3022	0.2957	0.0882	-0.0368	0.4435	1.6307
JH0078pax	1	1.2953	1.2767	1.2058	0.2609	1.2165	1.2786
JH0080pax	1	-2.1122	-1.1393	-1.0418	-0.7568	-1.5315	0.3507

JH0082pax	1	-0.6722	-0.5393	-0.0518	-0.2368	-0.3065	1.0857
JH0083pax	1	-1.3997	-0.0133	-0.3542	-1.2991	0.3115	0.7236
JH0086pax	1	0.2553	0.1667	0.0158	-0.7941	0.4015	1.1086
JH0092pax	1	-0.2647	1.6167	0.2158	0.2559	0.1565	1.3386
MH0001pa x	1	1.1653	1.7717	1.0908	1.1159	2.8015	1.9086
MH0009pa x	1	-0.4972	-0.0193	-0.7268	-0.5768	-0.3015	-0.3493
MH0012pa x	1	-0.1347	1.0017	0.3658	0.8559	0.9765	0.9186
MH0014pa x	1	0.8278	1.4457	0.8482	0.5432	3.0535	1.8007
MH0016pa x	1	-1.1672	-0.8793	-0.9168	-1.2168	-0.4165	-0.7243
MH0017pa x	1	0.3403	1.4267	0.5658	-0.0241	1.7565	2.0536
MH0018pa x	1	1.2128	0.7657	0.3232	0.3682	2.1235	0.7057
MH0021pa x	1	0.8103	0.2517	-0.3192	0.0709	1.6865	1.7086
MH0022pa x	1	0.6903	1.3667	0.6308	0.5459	1.2515	1.4236
MH0024pa x	1	0.2228	0.4757	-0.0568	-0.1768	0.0635	0.9057
MH0026pa x	1	-1.2897	0.0417	-0.4392	0.1059	-0.3935	-0.1914
MH0028pa x	1	-0.0272	0.3557	-0.1068	-0.8368	-0.0765	-0.0493
MH0029pa x	1	-0.0697	0.0167	0.0658	-0.6641	1.0215	0.3536
MH0035pa x	1	0.6603	2.0217	0.9458	0.7759	1.0965	1.4036
MH0037pa x	1	-0.1697	1.0717	-0.0342	0.1309	1.1665	1.6186
MH0038pa x	1	1.7453	1.5967	1.3108	1.4609	2.2365	2.3736
MH0039pa x	1	-1.1922	-0.3093	-0.1218	-0.5718	-0.0965	0.5557
MH0042pa x	1	-0.1522	0.0657	0.2332	-0.1318	-0.0815	0.9357
MH0050pa x	1	-1.4222	0.5507	-0.6818	-0.3468	0.8885	1.6307
MH0051pa x	1	-1.2197	-1.0683	-0.7092	-1.6041	-2.1735	-0.1814
MIP0004pa x	1	-2.1722	-2.1793	-1.4118	-1.1218	-0.9865	-2.2593
MP0013Ap	1	0.4028	1.2307	0.0782	0.2282	1.4535	0.1557

ax							
MP0014Bpax	1	-0.4347	0.6117	-0.5542	-0.0441	1.2765	-0.1964
MP0018Apax	1	-1.0022	-0.4193	-0.9668	-1.5668	-0.3165	-1.4293
MP0019Bpax	1	-0.6222	-0.2993	-0.3768	-0.6268	-0.3465	0.8757
MP0024pax	1	-1.2597	-0.2333	-0.4542	0.1409	1.3465	0.7386
NK2001pax	1	-0.8347	-0.1233	-0.6992	-1.5741	-0.0785	1.1036
NK2002pax	1	0.0203	-0.0183	0.1908	-0.4741	0.8115	0.9786
NK2003pax	1	-0.7372	0.0407	-0.3218	-0.2868	1.2085	-0.1993
NK2004pax	1	-0.9022	0.3107	-0.5118	-0.9568	0.5285	-0.3843
PB1829pax	1	0.3378	1.5057	0.0682	0.0782	1.5485	1.7407
PB1842pax	1	1.0953	1.3467	0.8708	0.2009	2.3265	0.9536
PB1872pax	1	0.3928	0.6507	0.5682	-0.5068	1.2035	0.1807
PB2857pax	1	-0.9422	0.5057	-0.3968	0.2982	-0.2165	0.8657
RC2919pax	1	2.0678	2.0357	1.6382	3.0282	2.8985	3.9757
RC3062pax	1	0.1453	0.5917	0.1408	0.3759	0.1365	0.3386
RC3277pax	1	-0.1122	0.1707	-0.0568	-0.0168	0.7285	0.2457
RC3297pax	1	0.2078	0.9457	0.4032	0.5332	2.7135	0.9807
RC3445pax	1	-0.8497	-0.1233	-0.3442	-0.7391	0.6765	0.3086
RC3467pax	1	2.0928	2.9557	1.5782	1.4332	2.8485	2.8457

Surprisingly, analysis of the data showed that RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 is present on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 10). The ranges of fold-change in the levels of RNA encoded by these genes normalized to levels of RNA encoded by IL2RB in blood of the training set subjects having colorectal cancer relative to the training set subjects not having any colorectal pathology are shown in Table 10.

Table 10. Sample training set ranges of fold-change in levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene					
	ANXA3	**CLEC4D**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**

Average normalized RNA level in subjects having colorectal cancer (ΔCt)	-0.30	0.42	-0.05	-0.12	0.79	0.66
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	0.46	0.99	0.39	0.65	1.42	1.25
Average RNA level fold-change	1.69	1.48	1.55	1.35	1.55	1.35
p-value for average RNA level fold-change	5.5E-09	5.5E-06	6.4E-07	2.5E-13	6.0E-06	2.7E-06
Maximum observed RNA level directional fold-change	14.43	12.01	6.83	11.46	13.58	11.36

As can be seen in Table 10, a test subject having a blood level of RNA encoded by ANXA3, normalized to a level of RNA encoded by IL2RB, which is 1.7 to 14.4 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 10, a test subject having a blood level of RNA encoded by CLEC4D, normalized to a level of RNA encoded by IL2RB, which is 1.5 to 12.0 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 10, a test subject having a blood level of RNA encoded by LMNB1, normalized to a level of RNA encoded by IL2RB, which is 1.5 to 6.8 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 10, a test subject having a blood level of RNA encoded by PRRG4, normalized to a level of RNA encoded by IL2RB, which is 1.3 to 11.5 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 10, a test subject having a blood level of RNA encoded by TNFAIP6, normalized to a level of RNA encoded by IL2RB, which is 1.5 to 13.6 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 10, a test subject having a blood level of RNA encoded by VNN1, normalized to a level of RNA encoded by IL2RB, which is 1.3 to 11.4 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Generation of logistic regression models for determining the probability that a test subject has colorectal cancer versus not having any colorectal pathology via measurement of levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB: Linear regression analysis of levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to IL2RB surprisingly showed that logistic regression models could be generated, based on blood expression levels normalized to IL2RB for all 63 possible combinations of one or more of these genes, for discriminating, with a ROC AUC of at least 0.67, between subjects having colorectal cancer and subjects not having any colorectal pathology. Examples of these logistic regression models are shown in Table 11. A logistic regression model based on ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 (Table 11, Model #128) was surprisingly found to enable discrimination between subjects having colorectal cancer and subjects not having any colorectal pathology with a ROC AUC of 0.80.

By way of example, Model #128 of Table 11 corresponds to:

$P = \{1 + e\text{^}-[(-0.196) + (-1.042)(L_{ANXA3}) + (0.393)(L_{CLEC4D}) + (1.272)(L_{LMNB1}) + (-1.837)(L_{PRRG4}) + (0.289)(L_{TNFAIP6}) + (-0.153)(L_{VNN1})]\}\text{^}-1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, where L_{ANXA3} is a ratio of a level of RNA encoded by ANXA3 to a level of RNA encoded by IL2RB in blood of the test subject, L_{CLEC4D} is a ratio of a level of RNA encoded by CLEC4D to a level of RNA encoded by IL2RB in blood of the test subject, L_{LMNB1} is a ratio of a level of RNA encoded by LMNB1 to a level of RNA encoded by IL2RB in blood of the test subject, L_{PRRG4} is a ratio of a level of RNA encoded by PRRG4 to a level of RNA encoded by IL2RB in blood of the test subject, $L_{TNFAIP6}$ is a ratio of a level of RNA encoded by TNFAIP6 to a level of RNA encoded by IL2RB in blood of the test subject, and L_{VNN1} is a ratio of a level of RNA encoded by VNN1 to a level of RNA encoded by IL2RB in blood of the test subject.

Further by way of example, Model #157 of Table 11 corresponds to:

$P = \{1 + e^{\wedge}\text{-}[0.288 + (-1.392)(L_{PRRG4})]\}^{\wedge}\text{-}1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, and L_{PRRG4} is a ratio of a level of RNA encoded by PRRG4 to a level of RNA encoded by IL2RB in blood of the test subject.

Table 11. Logistic regression models based on blood expression levels for any possible combination of one or more of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, normalized to IL2RB expression levels for determining the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer. ROC AUC values for the models are shown for the sample training set used to generate the models, as well as for an independent blind sample test set used to test the models. The models, listed in order of decreasing ROC AUC value for the training set, are based on expression levels determined via quantitative reverse transcriptase-PCR analysis using IL2RB as duplex partner for normalization. The form of these models is: $\mathbf{P = \{1 + e^{\wedge}\text{-}[K_0 + K_1L_1 + K_2L_2 + K_3L_3... + K_nL_n]\}^{\wedge}\text{-}1}$, where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology; K_0 is a constant; K_1 is a coefficient specific to a first gene; L_1 is a ratio of a level of RNA encoded by the first gene in blood to a level of RNA encoded by IL2RB in blood; K_2 is a coefficient specific to a second gene; L_2 is a ratio of a level of RNA encoded by the second gene in blood to a level of RNA encoded by IL2RB in blood; K_3 is a coefficient specific to a third gene; L_3 is a ratio of a level of RNA encoded by the third gene in blood to a level of RNA encoded by IL2RB in blood; K_n is a coefficient specific to an nth gene; and L_n is a ratio of a level of RNA encoded by the nth gene in blood to a level of RNA encoded by IL2RB in blood. No regression coefficients are specified for genes which are not included in the gene combination (indicated by "–") on which a given logistic regression model is based.

Logistic Regression Model #	No. of genes in Model	ROC AUC		Constant (K_0)	Gene-specific regression coefficient (K_n)					
		Training Set	Test Set		ANXA3	CLEC4D	LMNB1	PRRG4	TNFAIP6	VNN1
128	6	0.80	0.78	-0.196	-1.042	0.393	1.272	-1.837	0.289	-0.153
129	5	0.80	0.79	-0.298	-1.058	0.366	1.187	-1.854	0.285	–
130	5	0.80	0.79	0.034	-0.945	0.456	1.300	-1.715	–	-0.146
131	5	0.79	0.78	-0.070	-0.937	–	1.469	-1.774	0.336	-0.115

132	4	0.79	0.79	-0.065	-0.961	0.428	1.221	-1.733	–	–
133	4	0.79	0.78	-0.154	-0.955	–	1.394	-1.790	0.330	–
134	5	0.79	0.78	-0.305	-0.630	0.575	–	-1.632	0.311	-0.049
135	4	0.79	0.78	0.229	-0.799	–	1.537	-1.620	–	-0.097
136	4	0.79	0.79	-0.337	-0.645	0.562	–	-1.642	0.309	–
137	4	0.79	0.78	-0.058	-0.516	0.645	–	-1.493	–	-0.041
138	5	0.79	0.76	0.239	–	0.173	0.355	-1.782	0.144	-0.210
139	3	0.79	0.78	0.153	-0.817	–	1.474	-1.637	–	–
140	3	0.79	0.79	-0.085	-0.528	0.634	–	-1.503	–	–
141	4	0.79	0.76	0.128	–	0.280	–	-1.707	0.174	-0.162
142	4	0.79	0.76	0.337	–	0.216	0.413	-1.721	–	-0.203
143	3	0.79	0.77	0.229	–	0.355	–	-1.615	–	-0.144
144	4	0.79	0.76	0.279	–	–	0.492	-1.757	0.172	-0.189
145	4	0.78	0.76	0.109	–	0.128	0.225	-1.802	0.134	–
146	3	0.78	0.76	0.053	–	0.209	–	-1.747	0.157	–
147	3	0.78	0.76	0.416	–	–	0.607	-1.673	–	-0.173
148	3	0.78	0.76	0.206	–	0.169	0.285	-1.745	–	–
149	3	0.78	0.76	0.150	–	–	0.339	-1.781	0.156	–
150	2	0.78	0.77	0.153	–	0.285	–	-1.659	–	–
151	2	0.78	0.76	0.284	–	–	0.457	-1.703	–	–
152	3	0.78	0.76	0.123	–	–	–	-1.591	0.257	-0.078
153	3	0.78	0.77	-0.102	-0.352	–	–	-1.463	0.390	–
154	4	0.78	0.77	-0.130	-0.368	–	–	-1.474	0.388	0.037
155	2	0.78	0.76	0.082	–	–	–	-1.630	0.237	–
156	3	0.77	0.77	0.216	-0.179	–	–	-1.276	–	0.061
157	1	0.77	0.76	0.288	–	–	–	-1.392	–	–
158	2	0.77	0.77	0.267	-0.150	–	–	-1.256	–	–
159	2	0.77	0.76	0.296	–	–	–	-1.384	–	-0.011
160	5	0.73	0.75	0.162	-0.907	0.153	0.321	–	-0.073	-0.270
161	4	0.73	0.75	0.108	-0.930	0.130	0.296	–	–	-0.273
162	3	0.73	0.76	0.086	-0.818	0.185	–	–	–	-0.243
163	4	0.73	0.76	0.125	-0.793	0.206	–	–	-0.055	-0.238
164	4	0.72	0.75	0.208	-0.868	–	0.406	–	-0.046	-0.254
165	3	0.72	0.75	0.167	-0.888	–	0.380	–	–	-0.258
166	2	0.72	0.75	0.171	-0.698	–	–	–	–	-0.204
167	3	0.72	0.75	0.179	-0.691	–	–	–	-0.009	-0.203
168	3	0.72	0.76	-0.021	-0.870	0.134	–	–	-0.077	–
169	4	0.72	0.76	-0.012	-0.929	0.103	0.155	–	-0.087	–
170	2	0.72	0.77	-0.080	-0.907	0.102	–	–	–	–
171	1	0.72	0.76	-0.014	-0.827	–	–	–	–	–
172	2	0.72	0.76	0.031	-0.793	–	–	–	-0.043	–
173	3	0.72	0.76	-0.079	-0.957	0.074	0.122	–	–	–
174	2	0.72	0.76	-0.039	-0.932	–	0.178	–	–	–
175	3	0.72	0.76	0.026	-0.902	–	0.221	–	-0.068	–
176	3	0.71	0.72	0.514	–	–	-0.502	–	-0.191	-0.309
177	4	0.71	0.72	0.519	–	-0.024	-0.482	–	-0.186	-0.306

178	3	0.70	0.72	0.398	–	-0.097	-0.604	–	–	-0.319
179	2	0.70	0.73	0.361	–	–	-0.706	–	–	-0.333
180	2	0.70	0.70	0.727	–	–	–	–	-0.345	-0.451
181	3	0.70	0.71	0.701	–	-0.192	–	–	-0.256	-0.383
182	2	0.70	0.73	0.306	–	–	-0.769	–	-0.227	–
183	3	0.69	0.73	0.331	–	-0.085	-0.690	–	-0.208	–
184	1	0.69	0.73	0.102	–	–	-1.041	–	–	–
185	2	0.69	0.70	0.589	–	-0.367	–	–	–	-0.433
186	2	0.69	0.73	0.186	–	-0.170	-0.838	–	–	–
187	1	0.68	0.69	0.552	–	–	–	–	–	-0.671
188	2	0.68	0.72	0.548	–	-0.379	–	–	-0.331	–
189	1	0.67	0.70	0.549	–	–	–	–	-0.576	–
190	1	0.67	0.71	0.371	–	-0.649	–	–	–	–

Blind sample test set: Quantitative reverse transcriptase-PCR analysis of expression of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 in an independent test set of blood samples from 165 subjects having colorectal cancer and 171 subjects not having any colorectal pathology was performed as described above for the training set. The normalized RNA levels measured are shown in Table 12.

Table 12. Sample test set levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by IL2RB. Levels shown correspond to ΔCt.

Sample ID	Group	Gene					
		ANXA3	CLEC4D	LMNB1	PRRG4	TNFAIP6	VNN1
CD0036pax	0	-0.0922	-0.0443	-0.1868	-1.0168	0.5035	-0.0543
CD0053pax	0	1.1828	2.1407	1.5032	1.3032	2.9135	1.5907
CD0092pax	0	1.2028	0.9057	0.8232	0.6032	1.6285	0.2907
CD0108pax	0	-0.0522	-0.1893	0.2582	-0.1318	0.3385	0.2757
CD0122pax	0	0.5628	1.2857	0.5582	0.6382	2.0485	1.9357
CD0148pax	0	0.6778	2.0057	0.6732	1.4432	2.0335	1.5607
CD0192pax	0	0.6878	0.8157	0.7682	1.5882	0.7085	0.8907
CD0204pax	0	0.1978	0.6907	0.0782	-0.1418	1.0185	0.9557
CD0214pax	0	0.4478	0.1557	1.1682	1.1932	0.6235	0.6157
CD0237pax	0	0.3828	0.8707	-0.0168	0.0582	1.1685	0.8007
CD0238pax	0	0.2428	0.8957	0.3982	1.0232	1.5385	0.9657
CD0242pax	0	0.9528	1.3957	0.5082	-0.3818	0.9685	1.0307
CD0244pax	0	0.4928	0.3507	0.4182	0.8982	1.4535	-0.0493

CD0277pax	0	0.1453	1.7617	0.2358	0.4909	1.8265	0.1486
CD0282pax	0	-0.1572	0.2207	-0.2118	0.0632	0.7585	-1.2243
CD0295pax	0	0.1578	0.7957	0.5482	0.5332	1.1735	0.1907
CD0354pax	0	0.5178	0.9557	0.2432	1.0732	1.6235	1.0307
CD0367pax	0	0.7778	0.6857	0.5232	0.3432	1.8935	0.8457
CD0369pax	0	1.0328	2.1057	0.9982	1.9532	2.1885	1.7607
CD0398pax	0	2.1128	2.2157	1.6682	2.0432	3.7635	3.1407
CD0409pax	0	-0.2272	0.7757	0.0282	0.7082	0.5735	1.2357
CD0419pax	0	0.2503	0.9617	0.5758	0.3759	2.1815	-0.3114
CD0432pax	0	0.3628	0.5607	0.2532	0.0282	2.0485	0.4407
CD0437pax	0	-0.8872	-0.1793	-0.6918	-0.7768	0.4635	-0.1593
CD0472pax	0	-2.1022	-0.4543	-1.0718	-0.6968	0.0235	-0.4243
CD0482pax	0	3.2778	3.4857	2.2282	2.2532	4.6085	3.4507
CD0484pax	0	0.2778	1.1907	0.3932	1.3182	1.7635	0.4107
CD0507pax	0	1.4228	1.0757	1.0982	0.4282	2.4985	1.5357
CD0547pax	0	-1.6622	-0.1543	-0.5068	0.0632	0.1035	-0.3643
CD0571pax	0	0.9378	1.2407	1.0382	1.8282	2.3535	0.5757
CD0580pax	0	1.2978	1.6557	0.5582	0.4382	2.3585	1.2807
CD0583pax	0	-0.4472	-0.9493	-0.4968	-0.5218	0.7935	-0.6093
CD0603pax	0	0.6928	0.5507	0.1582	-0.0818	1.4135	1.2457
CD0604pax	0	0.0028	0.6557	-0.1218	-0.1268	1.6635	-0.1443
CD0619pax	0	-0.3072	0.2557	0.1532	0.5182	0.3285	0.8407
CD0637pax	0	0.3428	0.0357	-0.0618	0.3132	0.8935	0.6657
CD0667pax	0	-0.5672	-0.4993	-0.5168	-0.1568	0.0235	-0.2643
CD0670pax	0	3.0478	2.9307	1.7582	1.5882	3.3985	2.6957
CD0676pax	0	-0.7022	-0.6343	-0.5518	-1.0468	0.2485	0.0357
CD0687pax	0	1.4528	2.5807	1.6032	1.9382	1.9035	2.4357
CD0715pax	0	-2.1372	-1.5893	-1.0468	-0.7768	-0.3665	0.4757
CD0721pax	0	0.1778	1.1807	0.0382	0.0582	1.1935	0.7607
CD0726pax	0	-0.2472	-0.2193	0.0432	-0.0318	0.8985	-1.1393
CD0743pax	0	0.4178	-0.4243	0.2032	0.2782	1.6735	-0.0243
CD0786pax	0	0.6678	1.0807	0.6132	0.9682	1.8735	1.0607
CD0800pax	0	2.6478	2.7757	1.9282	2.4682	3.8585	3.0107
CD0829pax	0	-0.0722	0.4757	0.2082	-0.3318	0.5785	0.7957
CD0833pax	0	0.1378	-0.3693	0.0982	0.5032	0.8185	-0.2293
CD0840pax	0	-0.5072	0.4157	-0.2018	-0.5618	0.6035	0.1307
CD0843pax	0	0.2853	-0.1433	-0.2192	-0.5291	0.3415	0.2136
CD0937pax	0	1.2178	0.8507	0.9632	1.4432	2.6285	1.8457
CD1001pax	0	0.7553	0.8367	0.2758	-0.3541	2.7865	0.9686
CD1032pax	0	-3.0422	-2.3193	-0.7918	-0.7218	-1.1065	0.0557
CD1068pax	0	-0.1722	-0.0343	0.1382	0.5532	2.0935	-0.2243
CD1134pax	0	0.4253	1.2867	0.2608	0.4409	1.3565	1.9236
CD1269pax	0	0.0378	1.3507	0.1732	-0.2218	1.1735	1.1007
CD1270pax	0	0.8328	0.8557	0.6482	0.3532	1.4535	1.4157
CD1271pax	0	1.6778	2.4257	1.2282	0.6282	0.9885	1.8207
CD1278pax	0	0.2578	1.0757	0.5232	0.1582	1.2685	1.3507

CD1285pax	0	0.6903	0.3917	0.8458	0.3609	2.7765	0.8986
CD1313pax	0	1.7278	1.3757	0.8182	1.0282	2.8285	0.6057
CD1320pax	0	-0.8972	0.2757	-0.6068	-0.0668	0.1335	0.7907
CD1329pax	0	0.1903	-0.0983	0.2308	-0.3091	1.1115	0.8936
CD1349pax	0	-0.1622	0.5757	-0.3668	-0.9268	0.3935	0.5807
CD1401pax	0	-0.0397	-0.2933	-0.2492	0.2409	0.2715	0.2036
CD1428pax	0	2.0228	2.1257	1.1632	2.0382	2.5385	1.4807
CD1438pax	0	-0.1572	0.3757	-0.1418	0.3782	0.6935	-0.1493
CD1441pax	0	-0.6972	0.3307	0.0582	0.1132	0.7235	-0.3693
CD1458pax	0	0.2328	0.2407	0.9082	0.7332	1.8935	0.5707
CD1487pax	0	0.2378	1.9757	0.9582	1.6032	1.9785	0.5407
CD1559pax	0	-0.0022	0.8557	0.1632	0.3532	1.8685	1.0657
CD1561pax	0	1.1728	0.7557	0.6132	0.5432	1.8635	1.9307
CD1567pax	0	0.6928	1.4807	0.4982	1.2232	1.6035	1.2807
CD1627pax	0	-1.0072	-0.6693	-0.1868	0.2632	-0.4965	-0.2743
CD1708pax	0	1.3903	1.8417	1.1458	0.6909	2.4365	1.8636
CD1719pax	0	-0.4022	0.0407	-0.3068	-0.7568	0.1285	0.4657
CD1728pax	0	1.8578	2.0957	1.2732	2.0332	1.9635	3.0907
CD1741pax	0	-0.4922	-0.5493	-0.1868	-0.4618	1.0035	0.3257
PB0662pax	0	0.0003	0.3867	0.6908	0.6809	1.2815	-0.1464
PB0701pax	0	0.8803	1.5017	1.2058	2.1159	1.6765	3.1036
PB0790pax	0	0.4253	0.2867	0.5158	0.5459	0.1665	-0.2414
PB1222pax	0	-0.0272	0.4407	0.2932	-0.6868	-0.0465	0.8957
PB1260pax	0	-1.3447	-1.3983	-0.3742	-1.2441	-0.6585	-0.5814
PB1275pax	0	-0.7447	0.3767	-0.3092	0.2359	-0.1835	2.1786
PB1324pax	0	-0.1597	0.5667	0.4508	1.1109	1.7015	1.8886
PB1336pax	0	0.4853	0.6817	0.2158	-0.5991	1.1365	1.5136
PB1446pax	0	-0.9897	-0.0133	-0.1992	0.0159	0.7765	1.0086
PB1514pax	0	-1.2222	-0.2093	-0.3418	-0.4868	0.8185	-0.0293
PB1540pax	0	-0.7672	-0.2493	-0.2668	-0.0068	0.5185	0.8157
PB1700pax	0	0.5403	0.7517	0.5258	0.8759	1.3265	0.8836
PB1763pax	0	2.0953	2.5067	1.7958	2.6409	3.0115	1.9736
PB1785pax	0	0.9903	1.6717	0.6008	1.4309	1.3415	0.9486
PB1871pax	0	0.4853	0.3717	0.2008	0.3059	1.3365	1.4286
PB1918pax	0	2.6678	2.3457	1.4632	1.7882	3.8835	2.6107
PB1944pax	0	0.0028	-0.4843	0.4432	0.7482	0.5435	1.3507
PB1952pax	0	1.9703	1.9167	0.5508	1.8859	2.9865	2.0386
PB1973pax	0	2.7753	2.8667	1.9308	3.1009	3.7065	3.7736
PB1984pax	0	-2.2397	-1.7683	-1.8492	-1.7341	-1.4835	-1.3114
PB2005pax	0	1.4803	1.5917	0.8408	1.1159	3.3915	1.8386
PB2015pax	0	2.4703	1.9567	2.0908	3.2409	4.2865	2.5086
PB2024pax	0	0.8053	1.3967	0.8908	1.1359	2.6515	2.2286
PB2041pax	0	-0.5647	0.7517	-0.0692	0.1909	1.7565	0.1836
PB2062pax	0	2.4703	2.4517	1.7908	2.2809	3.3065	2.6786
PB2084pax	0	1.3553	1.0517	0.6808	1.5959	2.3965	1.4886
PB2130pax	0	0.4353	0.6717	0.0408	-0.1091	0.6315	0.6436

PB2179pax	0	0.6453	1.5017	0.5358	0.3559	0.7115	0.8686
PB2184pax	0	-0.8047	-0.1983	-0.3292	0.0859	0.2715	1.4886
PB2258pax	0	-0.0397	-0.9183	-0.5042	-0.4191	0.8415	-1.1164
PB2272pax	0	2.2653	2.2717	1.6408	1.7259	4.0015	1.8136
PB2342pax	0	2.9678	2.7557	1.1682	1.6732	2.4335	2.7607
PB2464pax	0	1.0003	1.6717	0.8458	0.4759	1.4465	3.2686
PB2516pax	0	0.1603	0.8067	0.4858	0.2109	0.6065	1.9036
PB2564pax	0	0.1253	1.3217	0.0258	0.3009	0.5815	0.7836
PB2634pax	0	0.0153	1.1567	0.8958	0.7009	2.5465	0.5586
PB2682pax	0	-1.2297	-0.1383	-0.5242	-1.4441	0.0415	-0.0114
PB2709pax	0	1.2978	1.7457	1.3832	1.9982	2.2535	1.3107
PB2711pax	0	-0.8797	-1.1033	-0.3892	-0.8391	0.5215	0.4736
PB2757pax	0	0.5353	1.6117	0.8508	0.6659	1.5865	1.9836
PB2809pax	0	-0.1722	0.9957	0.0032	-0.1768	0.6335	0.9057
PB2842pax	0	-0.5547	0.3867	-0.3492	0.0209	-0.2585	0.3486
PB2875pax	0	-0.0497	1.2967	0.3958	0.3959	1.2365	1.1736
PB2889pax	0	0.6453	1.9717	1.0808	1.4209	1.4015	1.5286
PB2909pax	0	-0.1372	-1.0543	-0.4368	-0.7268	0.2735	-0.3993
PB2924pax	0	0.7803	1.5167	1.1858	1.2159	1.3115	1.2786
PB2927pax	0	2.1453	0.8717	0.7158	0.1309	1.5815	2.1286
PB2931pax	0	0.2203	-0.3283	-0.8242	-0.8241	1.8315	-0.3664
PB2951pax	0	-0.0897	-1.6683	-1.0792	-0.2891	-0.3035	-0.9164
PB2974pax	0	-0.2547	0.8417	0.1958	0.2259	1.0515	2.2086
PB2978pax	0	3.1253	3.2667	2.2458	2.4059	3.7165	2.9886
PB2988pax	0	-1.5847	-1.3333	-0.7892	-1.1941	-0.2435	-0.3764
PB3014pax	0	1.3953	1.9017	1.2458	0.7959	2.3615	2.5236
PB3021pax	0	0.3053	2.1667	0.4108	0.9459	0.9015	0.7786
PB3032pax	0	-0.1547	0.4867	0.6658	0.0409	1.5065	1.1036
PB3163pax	0	0.3003	1.4117	0.5908	1.1459	2.4115	1.7336
PB3193pax	0	-0.0047	0.3717	0.0058	0.4559	1.1065	0.7036
PB3200pax	0	0.2653	1.0967	0.8608	1.0859	1.4265	1.5786
PB3226pax	0	0.3203	0.9467	0.4658	0.6709	1.9165	1.1536
PB3227pax	0	-0.0147	0.7317	0.4658	0.6559	2.0115	1.3936
PB3361pax	0	-0.8197	-0.1133	-0.5592	-0.9891	0.8715	-0.6564
PB3439pax	0	-1.2272	-1.8643	-1.1768	-1.2568	-0.9015	-1.7543
PB3445pax	0	1.6203	2.4017	1.5208	2.2859	2.7265	2.2836
PB3481pax	0	-0.0397	0.9167	0.3308	1.1359	0.5015	1.3636
PB3513pax	0	-0.0347	-0.2133	-0.5142	-0.6891	0.8765	-0.9214
PB3524pax	0	0.2103	-0.5733	0.1758	0.1859	1.2865	0.8486
PB3533pax	0	-0.3047	-0.7483	-0.2442	-0.0641	1.0465	-0.2664
PB3568pax	0	1.3153	1.4267	0.9858	1.0159	1.8915	0.8386
PB3582pax	0	1.4703	2.3517	1.7258	1.8509	3.3165	2.4236
PB3594pax	0	1.0753	1.2267	0.6958	1.2059	2.4615	1.2786
PB3806pax	0	-1.7122	0.1507	-0.6168	-0.1418	-0.2615	-0.3843
PB3828pax	0	-0.8197	0.3417	-0.2942	-0.6091	-0.2085	0.4136
PB3863pax	0	1.9153	1.8567	1.5808	1.4659	2.7065	2.5436

PB3877pax	0	2.1003	2.3217	1.6458	1.3909	3.4115	2.2186
RC2112pax	0	1.0653	2.1567	1.3008	1.7109	1.6115	2.0886
RC2236pax	0	1.1903	1.2017	1.0508	1.2159	1.5165	2.2136
RC2239pax	0	-0.2897	1.0767	1.0608	1.3759	0.5315	1.6386
RC2252pax	0	2.5353	1.9417	1.4658	1.9359	1.9515	2.7336
RC2338pax	0	1.1953	2.1167	1.1358	1.0609	2.2215	2.0636
RC2565pax	0	0.0753	1.1417	0.0458	1.2659	0.5465	2.0486
RC2615pax	0	-0.4847	0.1417	0.3558	0.5509	0.2765	1.1436
RC2699pax	0	1.1453	1.5167	0.8658	0.6759	1.7615	1.5636
RC2716pax	0	0.2703	0.4317	0.7308	1.1609	2.2865	0.9336
RC2728pax	0	-0.1697	1.2267	0.8108	0.5209	1.1265	0.4386
RC2768pax	0	1.2553	1.6867	0.9908	1.5259	1.8865	2.7936
RC2782pax	0	2.7703	3.4667	2.2058	2.3409	5.0215	2.7836
RC2869pax	0	1.3178	1.1907	0.7582	1.3432	2.3085	2.1657
RC2897pax	0	0.1853	0.7067	-0.0642	0.3409	1.1865	1.0436
RC2986pax	0	0.8953	0.9867	0.3458	0.4359	2.5115	1.4186
RC3191pax	0	1.4403	2.2267	1.2558	1.0409	1.9615	2.2036
RC3214pax	0	0.7903	1.6817	0.8258	0.8409	2.5365	1.1586
RC3379pax	0	1.3003	1.7467	1.0158	1.0509	2.4615	0.5686
RC3420pax	0	0.9153	1.0217	0.9258	1.6209	2.5815	0.4436
AN0001pax	1	-2.1122	-1.1143	-1.0218	-1.6018	-0.1515	-0.4493
AN0003pax	1	-3.9172	-2.1693	-2.9568	-1.2268	-2.2065	-2.5393
AN0007pax	1	-3.0572	-1.7593	-2.1818	-3.1218	-2.5615	-1.0493
AN0009pax	1	-0.3772	0.6607	0.0832	-0.0718	1.9985	1.0707
AN0012pax	1	0.5478	1.1207	0.3632	-0.0868	1.6385	1.6507
AN0013pax	1	0.2178	2.0007	0.9732	0.1332	2.7685	2.1157
AN0020pax	1	-1.8472	-0.4843	-1.1768	-1.7718	-1.3165	-0.3293
AN4011pax	1	-0.0972	0.8507	0.9782	0.5082	2.1785	0.9257
AN4012pax	1	1.6828	1.2857	1.1782	1.2582	2.7935	2.4957
AN4013pax	1	0.7928	2.0057	0.8132	0.6482	1.6385	1.8907
AN4014pax	1	-1.0472	0.2207	-0.1918	0.1232	0.4685	1.9757
AN4017pax	1	1.0003	1.3817	0.3358	0.2709	0.4565	1.2836
BE3001pax	1	-1.4472	0.2507	-0.3068	-0.6768	-0.8115	0.8657
CC0001pax	1	-0.2222	0.1107	-0.1668	-0.0168	1.2635	0.7907

CC0002pax	1	-0.5572	-0.8993	-0.6118	-1.9568	-0.2715	0.0957
CC0004pax	1	-1.2622	-1.0993	-0.4268	-0.1268	0.5335	0.6457
CC0005pax	1	0.8628	1.2457	0.6532	0.9132	1.8285	0.4607
CC0006pax	1	0.3128	0.4957	0.2332	0.5682	1.7235	2.2507
CC0007pax	1	-1.5122	0.0857	-0.2318	0.0032	-0.1365	0.3407
CC2001pax	1	-0.6672	1.0957	-0.0268	0.1382	0.9435	0.7757
CC2002pax	1	-0.6022	-0.9543	-0.6518	-1.5068	-0.2315	-0.3993
CD1111pax	1	1.5528	0.9857	1.1082	1.6382	2.0285	2.2057
CD1260pax	1	-0.4922	-0.5393	0.0532	-0.5368	1.1035	0.7257
CD1351pax	1	0.3978	0.4007	-0.0268	-0.3368	1.6485	0.5707
CD1571pax	1	0.6253	0.7717	0.9908	1.7909	2.5465	1.3386
CD1690pax	1	0.4278	0.5007	0.4682	0.5232	1.3985	-0.1993
DC0003pax	1	0.3378	0.8707	0.1182	0.0432	0.8135	1.8807
DC0005pax	1	0.6328	1.6957	0.6782	0.4432	1.5635	1.7007
DC0008pax	1	0.3628	0.7757	0.4632	-0.3718	1.6735	0.2907
DC0011pax	1	-0.1322	0.4157	0.5532	0.5082	1.5035	1.6757
DC0012pax	1	-1.2222	-0.4443	-0.6868	0.3132	-1.1115	-0.2343
DC1002pax	1	-1.2322	-0.7593	-0.3968	-0.3968	0.5535	0.3907
DC2005pax	1	-2.3922	-1.8993	-1.9468	-0.6968	-1.5515	-0.4343
DC2006pax	1	0.1778	0.4107	0.1982	-0.6518	1.0185	0.8557
DC3003pax	1	-0.2272	0.9507	0.1682	-0.4168	1.5985	1.8207
DC5006Apax	1	-0.0922	0.2057	0.2232	-0.3768	-0.1115	0.2157
DC5008Apax	1	-0.5972	-0.1043	-0.7018	-0.5168	0.8335	1.1557
DES1001pax	1	-1.8422	-0.8843	-1.1918	-1.4518	0.8185	-0.4143
DES1002pax	1	-0.6822	-0.8993	-0.0418	-0.5318	1.1235	-0.7943
JH0022pax	1	0.0828	0.5507	0.4282	0.5332	0.5935	1.0307
JH0076pax	1	-0.4872	-0.7793	-0.2418	-1.6768	-0.1715	0.1407
JH0085pax	1	-1.0822	-0.6293	-0.4668	-1.2268	-0.0365	-0.0193
JH0089pax	1	-0.1597	1.0267	-0.1642	-0.5691	0.7915	1.1336
JH0090pax	1	-0.7322	-1.0293	-0.4218	-0.0518	0.0435	0.4657
JH0091pax	1	0.1353	0.2617	0.2708	1.2709	1.2965	1.1536
JH0093pax	1	0.2428	1.4557	0.4232	-0.5368	1.5685	0.9107
JH0096pax	1	-2.0347	-0.6183	-1.4842	-0.6891	-2.2235	0.8736
JH0097pax	1	-0.4422	-0.5293	-0.0218	-0.7968	0.4985	-0.7193
JH0100pax	1	0.3803	1.2117	0.4858	0.6959	1.7015	1.0036
JH0101pax	1	0.8128	0.4507	0.6232	0.3482	1.6835	0.5857
JH0105pax	1	0.3878	1.1657	0.3682	-0.5768	1.7485	2.0007
JH0106pax	1	-0.6497	-0.2083	0.0308	-0.1191	0.8115	1.1536
JH0108pax	1	-0.0772	0.6557	0.3282	-0.0768	0.8485	1.1157
JH0109pax	1	0.9803	1.9517	0.7158	0.2559	1.7615	2.2986
JH0110pax	1	-0.5072	0.2307	-0.1668	-0.6018	-0.3515	0.7807
JH0111pax	1	0.7503	1.7717	0.4808	1.8809	2.4715	1.1486

JH0113pax	1	-0.3047	0.5867	0.3308	-0.8441	0.5715	0.1886
JH0114pax	1	-2.0472	-1.6493	-1.3618	-0.6518	-1.7715	-2.1743
JH0116pax	1	-0.2772	1.1207	0.2182	0.6082	0.7885	0.7457
JH0117pax	1	-1.6972	-0.6243	-1.0418	-0.8018	-0.1765	0.4257
JH0118pax	1	0.3503	-0.0433	0.5258	-0.0441	1.1065	0.4236
JH0120pax	1	-0.3797	0.2467	-0.0792	-1.2341	1.4265	0.0686
JH0123pax	1	-1.8597	-0.9733	-0.7492	-0.5891	-0.8185	-1.2464
JH0126pax	1	-1.7822	-0.3243	-0.7168	-1.3618	-0.6665	0.2307
JH0127pax	1	-0.3897	1.0367	0.4308	0.7759	0.6415	0.6086
JH0129pax	1	0.3903	1.2817	0.6808	1.0259	2.6865	1.8886
JH0130pax	1	-0.9022	-0.3543	-0.7818	-0.9818	-0.4465	0.2657
JH0131pax	1	-0.4922	-0.5243	-0.5968	-1.3968	-0.8715	0.2057
JH0132pax	1	-0.3897	0.1117	-0.0742	0.3959	0.4615	0.1436
JH0135pax	1	-1.3622	-1.6143	-1.2368	-1.1018	-1.2465	-1.4743
JH0136pax	1	-2.6172	-1.9043	-1.3118	-1.4768	-1.1965	-2.0743
JH0137pax	1	-0.1372	0.9407	-0.3768	-0.6168	0.7685	0.5507
JH0138pax	1	-0.5622	0.1957	0.0532	-0.3068	0.2285	0.2757
JH0139pax	1	-0.7247	-0.6583	-0.5792	-1.1191	-0.4935	-0.8464
JH0142pax	1	-0.4547	0.7017	0.3608	0.4459	0.7815	-0.1964
JH0144pax	1	0.3128	2.3157	0.8682	-0.1368	2.0135	1.2707
JH0147pax	1	0.3778	1.4257	0.4532	0.5232	2.9535	0.7407
JH0149pax	1	0.5528	1.2407	0.3682	0.1432	2.5535	0.9357
KW0002pax	1	-0.4072	0.4307	-0.1868	-0.4968	0.6785	1.3907
KW0003pax	1	0.0253	1.3217	0.7908	-0.0691	0.1415	3.0886
MH0053pax	1	2.2253	2.3967	1.2558	0.6209	3.2815	2.1886
MH0057pax	1	-0.6947	-0.5333	-0.4792	-0.5041	0.5915	-0.5264
MH0059pax	1	-2.8497	-2.1083	-2.1892	-1.5691	-0.3235	-1.1764
MH0062pax	1	-0.9697	-0.1633	-0.0592	-0.4891	0.5065	0.3186
MH0065pax	1	-1.7097	-1.6233	-0.8042	-0.9491	-0.6235	-1.1314
MH0066pax	1	-1.4297	-0.9733	-1.0642	-0.8041	-0.5235	-0.9314
MH0068pax	1	2.4828	2.4407	1.7882	1.6982	3.0035	1.0707
MH0070pax	1	0.1703	0.8467	0.5808	0.3859	1.4015	1.1036
MH0073pax	1	-1.5622	-0.8493	-1.3868	-1.4018	-0.1715	-0.7993
MH0074pax	1	-1.0422	-1.1393	-0.6218	-0.6218	0.7535	-1.2193

MH0076pax	1	0.2653	1.8167	0.0658	-0.4241	2.0165	2.0386
MH0077pax	1	-0.2772	0.3357	-0.2418	-0.6218	0.2935	0.4157
MH0078pax	1	-1.2497	-0.0583	-0.6992	-1.7091	-0.7685	1.0236
MH0079pax	1	0.6153	0.7767	0.5608	-0.0241	0.6065	1.1786
MH0080pax	1	-0.1597	0.2867	0.5258	0.3709	1.5765	0.6186
MH0081pax	1	0.1403	1.2367	0.1658	-1.1941	1.7615	0.7686
MH0082pax	1	0.8203	1.4817	0.4558	-0.1441	1.6365	0.7336
MH0083pax	1	1.5778	1.7007	0.9332	1.2532	2.2185	1.6807
MH0087pax	1	-0.9922	0.9707	-0.0668	0.5032	1.4985	0.6507
MH0088pax	1	-0.2172	0.8457	0.3582	-0.1868	0.8535	0.5157
MH0089pax	1	-2.2197	-1.5133	-1.0292	-1.5141	-0.8685	-0.3364
MH0090pax	1	-0.9247	0.3217	-0.2792	-0.6841	0.0065	-0.4964
MH0095pax	1	-2.1147	-1.5633	-1.4142	-1.8041	-1.0985	-0.9514
MIP0002pax	1	-1.8047	-0.3533	-0.6842	-0.1141	-0.0685	0.4836
MIP0003pax	1	0.0778	0.1157	-0.1818	0.0282	0.7585	-0.1643
MIP0005pax	1	-2.2797	-1.3883	-1.6292	-1.1741	-0.8035	-1.7414
MIP0008pax	1	0.5053	0.8367	0.0008	-0.2191	1.8415	0.7086
MIP0009pax	1	-1.3122	-1.1793	-1.2268	-1.4768	-0.6215	-1.0043
MIP1007pax	1	-1.1547	-0.4633	-0.4792	0.1859	0.2515	-1.4864
MIP1009pax	1	-2.9997	-1.6083	-2.0442	-1.4391	-0.7485	-1.1164
MIP1011pax	1	-0.6497	-0.7283	-0.8992	-1.0491	0.3015	-0.8914
MIP1013pax	1	-0.0222	0.8707	0.0282	0.0432	0.7335	1.4007
MIP2002pax	1	0.8603	1.4317	0.7358	0.4159	1.6165	1.3386
MIP2003pa	1	-0.2947	0.3567	0.2508	0.6959	1.8515	0.8486

x							
MIP2006pa x	1	-0.3622	0.7457	0.0432	0.5432	0.8035	0.3157
MIP3003pa x	1	-2.5772	-1.5843	-2.1418	-1.4368	-1.7415	-1.3193
MIP3004pa x	1	-0.9222	-0.5393	-0.4618	-0.3918	0.6435	-0.6943
NK1001pa x	1	0.4828	1.0657	0.0782	0.1832	1.9635	0.9307
NK1003pa x	1	-0.9747	0.1017	-0.1192	-0.3691	0.4365	0.4536
NK1004pa x	1	-0.7947	-0.5133	-0.4642	-0.8441	0.6715	0.0186
NK1005pa x	1	-0.1597	1.5217	0.8058	0.4809	2.0815	0.9936
NK1008pa x	1	-1.6222	0.1407	-0.5918	-0.2818	-0.0215	0.2257
NK1009pa x	1	1.6828	1.5207	0.7182	0.4582	2.3135	1.0907
NK2005pa x	1	-1.5347	-0.9483	-0.6192	-0.8041	-1.9435	-0.0114
NK2006pa x	1	-1.9272	-1.2543	-1.7168	-1.1568	-0.7815	-1.6093
NK2007pa x	1	0.1978	0.4957	0.1282	0.6782	1.0285	-0.0693
NK2008pa x	1	-1.9022	-1.2193	-1.0068	-1.3468	-0.0615	-1.4393
NK2009pa x	1	-0.4097	0.3167	0.0658	-0.7691	1.5165	-0.0614
NK2010pa x	1	-1.1147	-0.5983	-0.4692	-0.8091	-0.3935	-0.7364
NK2014pa x	1	0.6753	1.6317	1.0258	1.0759	2.0515	1.1686
NK2015pa x	1	-0.6222	0.6307	0.0482	-0.4318	1.6935	1.3107
NK2016pa x	1	-0.4297	0.2167	-0.2092	0.0659	1.6815	0.4936
NK2018pa x	1	-1.9522	-1.1093	-0.8468	-0.9018	-0.2715	-0.9843
NK5008pa x	1	-1.4522	-1.6693	-1.3418	-1.5618	0.4085	-1.2843
OL0003pax	1	-1.2897	-0.5083	-0.9542	-0.7241	-0.1385	-0.3214
OL0014pax	1	-2.3397	-2.4483	-1.7342	-1.7191	-1.8585	-1.0564
OL0017pax	1	-1.0297	-1.0083	-0.6692	-0.5541	0.6465	0.3036
OL0026pax	1	-2.2947	-1.4533	-2.0092	-1.8291	-0.6635	-0.4364
OL0034pax	1	-1.3647	-0.8333	-1.2992	-1.7341	0.1615	0.0536
OL0041pax	1	-2.2297	-1.6183	-2.1492	-2.8641	-1.4835	-2.1464

OL0043pax	1	-0.8772	-0.6193	-0.7268	-1.2568	0.0285	-0.5693
OL0052pax	1	-1.3047	-1.2733	-0.4242	-0.5541	-0.2135	-0.5464
OL0056pax	1	-0.2972	-0.9943	-0.0518	-0.6268	1.5235	0.6557
OL0057pax	1	-0.8447	-0.4883	-0.7942	-0.8191	-0.1335	-0.1664
OL0058pax	1	-1.1572	-1.2643	-1.1518	-0.9918	-0.1265	-1.8993
OL0059pax	1	-1.1947	-0.0983	-0.5492	0.0109	0.0115	0.0936
OL0060pax	1	-1.8622	-1.6843	-1.4368	-2.0668	-1.6665	-1.0693
OL0062pax	1	0.3003	0.2817	0.3108	0.0709	1.7915	1.3986
OL0063pax	1	-1.3172	-0.8843	-0.8068	-0.5168	-0.3665	-0.7093
OL0064pax	1	0.3203	0.9317	0.7908	0.6409	1.8015	0.7186
OL0065pax	1	0.4578	0.7257	0.6832	0.6982	1.8085	0.6357
OL0066pax	1	-0.2722	0.5757	-0.0618	0.4232	0.6785	1.0357
OL0068pax	1	-1.9622	-0.7143	-1.3218	-1.1918	-0.5765	-1.0593
OL0070pax	1	-1.3622	-0.6193	-1.2868	-2.0718	-0.3665	-1.5243
OL0071pax	1	-0.6897	0.1217	-0.3542	0.1559	0.7515	0.8136
OL0072pax	1	-1.1047	-0.4033	-0.4392	-1.1791	0.2315	-0.9964
OL0073pax	1	-2.6897	-1.9933	-1.1642	-1.1641	0.3565	-0.5114
OL0074pax	1	-1.4447	-0.7883	-0.9142	-0.6891	1.0865	-0.1364
OL0075pax	1	-0.8322	-0.0343	-0.3218	0.3782	0.8585	0.5457
OL0077pax	1	-1.0747	-0.5933	0.1708	0.3059	0.2265	0.2036
OL0078pax	1	-2.2597	-1.8983	-1.1942	-1.1441	-0.8135	-0.9764
OL0079pax	1	-1.1797	-0.7633	-0.9442	-1.2641	-0.8335	-0.0214
OL0080pax	1	-0.0772	0.4507	0.2882	0.3882	0.3985	0.5357
PB3545pax	1	-0.3222	1.4657	0.0382	0.4682	1.1435	0.6807
PB3890pax	1	-0.4397	-0.2383	0.4108	0.7759	0.1265	0.1686

The test set results confirmed the surprising finding based on the training set that ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 each express RNA on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 13). The ranges of fold-change in the levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of the test set subjects having colorectal cancer relative to the test set subjects not having any colorectal pathology are also shown in Table 13.

Table 13. Sample test set ranges of fold-changes in levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene

	ANXA3	CLEC4D	LMNB1	PRRG4	TNFAIP6	VNN1
Average normalized RNA level in subjects having colorectal cancer (ΔCt)	-0.63	0.01	-0.27	-0.38	0.56	0.28
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	0.45	0.85	0.45	0.59	1.47	1.04
Average RNA level fold-change	2.11	1.80	1.65	1.95	1.88	1.69
p-value for average RNA level fold-change	1.2E-17	7.3E-12	1.5E-15	2.5E-19	5.4E-12	2.6E-10
Maximum observed RNA level directional fold-change	20.61	9.85	10.64	13.07	16.37	11.93

As can be seen in Table 13, a test subject having a blood level of RNA encoded by ANXA3, normalized to a level of RNA encoded by IL2RB, which is 2.1 to 20.6 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 13, a test subject having a blood level of RNA encoded by CLEC4D, normalized to a level of RNA encoded by IL2RB, which is 1.8 to 9.85 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 13, a test subject having a blood level of RNA encoded by LMNB1, normalized to a level of RNA encoded by IL2RB, which is 1.65 to 10.6 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 13, a test subject having a blood level of RNA encoded by PRRG4, normalized to a level of RNA encoded by IL2RB, which is 1.95 to 13.1 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 13, a test subject having a blood level of RNA encoded by TNFAIP6, normalized to a level of RNA encoded by IL2RB, which is 1.9 to 16.4 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 13, a test subject having a blood level of RNA encoded by VNN1, normalized to a level of RNA encoded by IL2RB, which is 1.7 to 11.9 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Furthermore, the test set results confirmed the surprising finding based on the training set that logistic regression models based on blood expression levels for any of the 63 possible combinations of one or more of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, each of which normalized against expression levels of IL2RB, can be used to discriminate, with a ROC AUC of at least 0.66 (Table 11), between subjects having colorectal cancer and subjects not having any colorectal pathology. As such, the novel logistic regression models listed in Table 11 can be used to determine the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, based on blood levels of expression of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and/or VNN1 normalized to those of IL2RB.

EXAMPLE 4

Determination of the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer using blood levels of RNA encoded by the colorectal cancer markers: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to those of ACTB.

A blood sample from a test subject is analyzed for levels of RNA encoded by ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, as described in Example 1, above, thereby generating test data. Logistic regression model #1 of **Table 6** is applied to the test data, thereby providing the probability that the test subject has colorectal cancer as opposed to not having any colorectal pathology.

EXAMPLE 5

Determination of the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer using blood levels of RNA encoded by the colorectal cancer

markers: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to those of IL2RB.

A blood sample from a test subject is analyzed for levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 as described in Example 1, above, thereby generating test data. Logistic regression model #64 of Table 11 is applied to the test data, thereby providing the probability that the test subject has colorectal cancer as opposed to not having any colorectal pathology.

EXAMPLE 6

Measurement of blood levels of RNA encoded by a combination of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 relative to the level of RNA encoded by IL2RB can be used to determine the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology

MATERIALS AND METHODS:

Refer to "General materials and methods", above.

EXPERIMENTAL RESULTS:

Sample training set:

Discovery of significantly different levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, VNN1, TNFAIP6 normalized to IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology: Quantitative reverse transcriptase-PCR analysis of gene expression in a training set of blood samples from 112 subjects having colorectal cancer and 120 subjects not having any colorectal pathology (subset of samples listed in Table 9 of Example 3, above), using IL2RB as duplex partner for normalization of gene expression levels was performed. The normalized RNA levels measured are shown in Table 14.

Table 14. Sample training set levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by IL2RB. Levels shown correspond to ΔCt.

Sample ID	Group	Gene

		ANXA3	CLEC4D	LMNB1	PRRG4	TNFAIP6	VNN1
CD0011pax	0	1.0600	1.5250	1.3250	1.1000	2.3500	2.7750
CD0012pax	0	1.3600	1.6300	0.8600	0.8500	1.8350	2.7300
CD0030pax	0	1.4100	1.4500	0.9800	1.2850	1.0250	1.9600
CD0063pax	0	2.5700	3.3050	1.7550	1.9950	3.6000	3.2500
CD0077pax	0	-0.2350	0.7700	0.1500	0.3000	0.3900	1.1650
CD0078pax	0	1.5150	2.2800	0.7550	0.6750	2.6250	1.3750
CD0085pax	0	0.5750	1.6050	0.6450	0.9450	2.5450	0.7200
CD0117pax	0	0.9750	2.3900	0.9250	2.0600	2.4600	0.9400
CD0167pax	0	-0.9750	0.2000	0.4600	0.6600	1.6250	0.5800
CD0249pax	0	-0.5100	-0.2750	-0.5200	0.3200	0.2750	0.6400
CD0286pax	0	-0.2850	1.0900	0.2500	0.2050	0.3550	0.3300
CD0297pax	0	0.0300	0.4850	0.4700	-0.0300	0.3900	1.0050
CD0323pax	0	1.9000	1.9500	0.8350	1.4850	2.6400	3.4450
CD0445pax	0	0.6600	0.8250	0.3000	0.3750	1.4100	1.4350
CD0463pax	0	-0.0850	1.7650	0.6000	0.8550	1.3700	1.5650
CD0491pax	0	-0.5550	0.0650	0.1100	0.5450	0.9000	0.2150
CD0496pax	0	1.2050	2.8450	1.2400	1.9200	1.4650	1.3450
CD0501pax	0	1.1050	1.9100	1.1100	1.0600	2.8650	1.4900
CD0504pax	0	-0.7750	-0.2850	-0.1500	0.6100	-0.1950	0.3350
CD0573pax	0	1.8100	1.2350	0.7700	0.8300	2.2650	1.8500
CD0578pax	0	1.8200	1.9800	0.9550	1.0450	2.0700	2.2950
CD0639pax	0	0.2950	0.7900	0.7450	-0.2600	1.2000	1.7900
CD0645pax	0	-1.0950	-0.6000	-0.7700	-0.6250	-0.0200	-0.1800
CD0679pax	0	0.2300	1.5950	0.5200	0.3350	1.8800	1.8750
CD0685pax	0	0.5250	1.7300	0.4350	0.9850	1.6850	1.0550
CD0716pax	0	1.9900	2.4700	0.8200	0.5250	1.4050	2.1600
CD0749pax	0	0.1600	1.0600	0.1200	0.3600	1.6800	0.8350
CD0760pax	0	-2.3750	-1.0500	-1.7400	-0.9100	-0.8100	-0.6700
CD0811pax	0	1.9250	2.3300	0.7400	0.8900	0.9700	1.0100
CD0848pax	0	1.0900	1.6300	1.4050	1.3850	1.9400	2.4750
CD0924pax	0	0.3450	0.7500	0.2250	-0.1100	0.5050	0.3050
CD1066pax	0	-0.2050	0.0950	-0.1200	-0.1750	1.3650	0.1800
CD1073pax	0	0.3050	0.1350	0.3150	0.9350	1.0850	0.3400
CD1075pax	0	0.0300	0.9000	0.4100	1.5200	1.6000	0.8400
CD1089pax	0	-1.3250	-0.2000	-1.1200	-0.8700	-0.1650	-0.2550
CD1116pax	0	-0.3850	-0.3700	-0.4500	0.0001	1.0600	0.1750
CD1120pax	0	-1.1350	-0.0400	-0.7450	0.0150	1.0100	-0.5700
CD1198pax	0	0.2950	0.4300	0.6350	0.5200	0.7850	0.6000
PB1179pax	0	1.2100	1.2700	1.1550	1.2700	2.6850	1.7300
PB1277pax	0	0.6600	1.3300	0.2500	0.6650	1.6000	0.5900
PB1301pax	0	-2.1150	-1.4000	-1.3850	-1.1000	-1.2350	-1.7950
PB1315pax	0	-1.3350	0.4800	-0.3200	-0.1800	0.0600	1.0750
PB1345pax	0	0.0150	0.5500	0.5950	0.8350	0.3650	1.9650
PB1520pax	0	0.9250	2.0050	0.7850	-0.1800	1.4100	1.8550

PB1574pax	0	1.2150	2.0550	1.2150	0.9500	1.3300	1.7150
PB1783pax	0	1.7400	1.8450	1.3600	1.3450	2.3150	1.8150
PB1799pax	0	0.7800	1.1900	0.6900	1.1150	2.3400	0.9800
PB1811pax	0	1.0950	1.6200	1.1050	1.4050	1.5800	1.2650
PB1830pax	0	0.3450	0.8850	0.5650	0.2700	1.3300	2.4950
PB1833pax	0	-0.0150	0.7050	0.0700	0.3150	0.5200	1.2600
PB1843pax	0	0.8750	0.9400	0.4750	0.8500	-0.3150	1.6500
PB1851pax	0	0.2450	-0.0450	0.1250	0.1650	2.6550	1.3150
PB1919pax	0	1.3100	1.8550	0.6050	1.5350	2.0800	2.2100
PB1922pax	0	-0.1700	0.8350	-0.0700	0.8450	1.6350	0.5700
PB1924pax	0	0.0950	0.5700	-0.0750	0.2150	1.0050	1.3000
PB1937pax	0	1.5250	2.5500	1.3500	3.0050	2.7050	2.3350
PB1964pax	0	0.6950	2.7450	1.0200	1.6750	2.6250	3.0550
PB2027pax	0	0.0900	0.5100	0.3500	1.3200	1.5250	0.7550
PB2029pax	0	0.5250	1.0200	0.6150	0.4300	2.2750	1.4350
PB2073pax	0	0.6000	1.0100	0.9000	1.8550	1.7200	1.2800
PB2099pax	0	-0.1500	-0.0950	0.1350	0.3250	0.0950	0.6700
PB2100pax	0	1.2350	1.3800	0.8950	1.5600	2.3100	1.4450
PB2132pax	0	0.5100	1.2400	0.1700	0.5100	1.9950	1.4750
PB2168pax	0	1.1400	1.4600	0.6600	1.0000	2.1650	1.2450
PB2192pax	0	-0.0050	0.4950	-0.1450	-0.4800	0.8350	1.5800
PB2196pax	0	0.8850	1.7250	0.9850	1.9050	2.2550	1.1350
PB2200pax	0	0.8550	1.3850	0.2350	0.3050	0.9050	0.4400
PB2213pax	0	1.8550	2.0000	0.9300	0.5300	2.9900	1.5850
PB2224pax	0	-0.3850	0.4250	-0.1400	0.1000	1.8950	0.9750
PB2228pax	0	2.0300	2.2200	1.8000	2.0050	4.0300	3.0800
PB2229pax	0	0.0050	-0.0800	0.2000	-0.6150	0.9150	0.2550
PB2277pax	0	1.3400	1.0050	0.7550	0.3700	1.3100	1.7800
PB2297pax	0	0.2900	0.8050	-0.0900	-0.0850	0.5250	-0.2800
PB2312pax	0	1.5250	2.1700	1.6550	1.2050	2.2900	2.1700
PB2398pax	0	-0.3800	0.2250	0.0150	-0.4700	0.1050	1.4250
PB2409pax	0	0.3950	1.0600	0.4950	0.5050	1.1550	1.7350
PB2414pax	0	3.0050	2.6050	1.4550	2.3150	3.9600	2.1150
PB2467pax	0	0.4800	1.0800	0.3500	0.3600	2.1300	1.0850
PB2473pax	0	0.2350	0.8600	0.2850	0.8850	1.0100	1.5950
PB2512pax	0	0.8200	1.8950	1.1800	0.8200	2.0650	2.3750
PB2568pax	0	-0.2950	0.1900	-0.0900	0.5850	1.4750	1.1700
PB2571pax	0	0.5800	1.2800	0.7500	0.4300	2.0650	2.1050
PB2824pax	0	0.8400	1.3650	0.8000	1.3950	2.0150	1.7750
PB2880pax	0	1.2500	1.4400	0.8850	-0.0600	2.2550	1.8100
PB3088pax	0	1.3800	1.2900	0.8550	0.6050	2.9200	2.0800
RC0882pax	0	-0.0150	1.2350	0.2800	0.3700	1.7700	1.6550
RC0888pax	0	-1.0450	-0.4250	-0.3400	0.0550	0.4950	0.1900
RC0968pax	0	-0.6900	-0.4750	0.2700	1.5500	1.0250	2.3500
RC2114pax	0	-0.2000	0.9600	0.3300	0.6550	0.4550	2.0900
RC2238pax	0	1.3450	2.0600	0.8800	1.8300	2.7050	3.1100

RC2681pax	0	0.1100	0.6300	0.2200	0.2550	0.2550	0.6550
RC2703pax	0	1.8000	2.1000	1.0500	1.5250	1.4250	1.5350
RC2749pax	0	0.0900	0.7750	-0.0850	0.0500	1.2550	1.2500
RC2750pax	0	-1.5150	-1.0750	-0.9000	-0.2200	0.0700	-0.5400
RC2756pax	0	1.6800	1.3850	1.0550	1.4600	1.9450	2.5150
RC2771pax	0	-0.8450	0.4950	-0.6450	-0.4150	1.1200	1.2750
RC2790pax	0	1.0850	1.1500	0.6150	0.8950	1.3350	1.5650
RC2792pax	0	1.0100	0.6250	0.6300	1.0950	1.9150	1.3550
RC2808pax	0	0.4850	1.4600	0.2700	0.5100	0.6550	1.0150
RC2822pax	0	0.4750	0.8350	-0.0900	0.3350	2.2400	0.4750
RC2834pax	0	-0.7350	0.2100	-0.6700	1.5700	2.1300	-0.3050
RC2871pax	0	0.6150	1.1650	0.9250	1.3150	2.4200	2.2250
RC2879pax	0	-0.4050	0.2050	-0.2400	0.5300	0.5250	0.0900
RC2892pax	0	-0.1500	0.1200	-0.4050	0.2750	1.6700	0.9100
RC2895pax	0	1.8700	2.2100	1.3750	1.6500	1.5650	2.2500
RC2921pax	0	1.2850	1.4150	0.9900	1.4400	1.9950	2.0900
RC2958pax	0	0.9250	1.0000	0.2300	0.0001	0.2700	1.2250
RC3022pax	0	0.1450	-0.0150	0.1200	0.7850	1.3950	0.2450
RC3112pax	0	1.0250	1.2350	0.3150	0.2650	2.3150	0.8700
RC3146pax	0	-0.3350	-0.3450	-0.6200	0.8250	0.9650	-0.3750
RC3184pax	0	2.4850	2.8750	1.3900	1.6250	2.5600	2.3950
RC3232pax	0	-0.2550	0.7850	-0.2900	0.6900	-0.1250	2.6700
RC3324pax	0	0.3650	1.0800	0.1200	0.6100	1.5200	0.1250
RC3327pax	0	0.3600	0.0950	0.2250	-0.0500	1.4550	1.9700
RC3355pax	0	-0.1850	0.4200	-0.4950	-0.3100	1.2150	0.3400
RC3380pax	0	-0.6450	0.3950	-0.5700	-0.3000	0.4950	-0.2300
RC3413pax	0	0.2750	0.8950	0.1250	-0.3400	0.5050	2.3050
RC3421pax	0	0.3550	0.4600	0.3900	0.4400	0.1300	0.2750
RC3468pax	0	-0.3600	-0.2800	-0.4100	-0.5750	0.9000	0.0350
RC3498pax	0	-0.3150	-0.7750	-0.7050	-0.2900	0.7750	-0.1800
CC0003pax	1	-1.2200	-0.2350	-0.8100	-0.6450	1.0450	-0.6850
CD0157pax	1	1.2350	1.0300	0.7450	0.9100	2.5050	2.3600
CD0164pax	1	0.3150	0.8550	1.0100	1.2550	2.7950	1.8100
CD0256pax	1	-0.4000	0.2050	0.1950	1.0400	1.2350	0.3300
CD0322pax	1	-0.9950	-0.2450	-0.7150	-0.1400	0.6750	1.2850
CD0356pax	1	-0.4950	-0.8850	-0.4500	-0.5650	-0.1000	-0.8600
CD0371pax	1	0.2350	1.0650	0.0500	-0.1800	0.9500	-0.0100
CD0629pax	1	0.1350	0.9850	0.7900	1.4800	0.5100	1.3850
CD1050pax	1	1.1750	0.3600	0.6850	1.0250	1.7150	1.3150
DS0003pax	1	-1.6350	-0.5200	-1.1950	-0.4900	-0.0650	-0.0600
FC0005pax	1	-0.1950	-0.0950	0.0900	-0.0450	0.1950	1.4100
FC0011pax	1	-0.0650	0.1250	0.1700	0.0800	1.1250	0.4950
FC0012pax	1	-2.2350	-0.1250	-1.0650	-0.9850	-0.0150	-0.2000
JGA0001pa x	1	-2.4550	-1.7500	-1.8250	-0.8650	-1.4800	-1.4400
JH0002pax	1	0.3150	0.7350	0.2850	0.1350	1.1700	0.3000

JH0003pax	1	0.0550	0.0650	-0.3850	-0.6250	-0.1450	0.7100
JH0004pax	1	-0.0550	-0.0050	-0.0250	-0.2100	1.4050	1.0300
JH0005pax	1	0.2950	1.3450	0.3700	0.4300	1.8650	1.2700
JH0006pax	1	-0.4300	0.4450	-0.0050	-0.0850	1.2650	-0.0600
JH0007pax	1	-2.4350	-1.9900	-1.3150	-0.1700	0.1250	-0.9150
JH0008pax	1	0.9050	2.5850	0.6250	1.1850	2.3350	1.0050
JH0009pax	1	-1.0700	-1.3450	-0.3350	-0.9650	-0.6700	0.1550
JH0010pax	1	-0.7650	0.0800	-0.1650	-0.0750	0.0300	-0.6650
JH0012pax	1	-0.2150	0.1900	0.1000	-0.2150	0.4400	0.6950
JH0013pax	1	-0.1200	0.3750	-0.0300	0.1150	2.2800	0.9200
JH0014pax	1	1.0050	0.8950	0.1500	-0.3400	1.6200	2.2850
JH0016pax	1	0.7850	1.1950	0.8600	0.4350	0.6450	1.0350
JH0018pax	1	-0.9850	-0.0250	-0.1450	-0.2900	0.0750	0.6250
JH0019pax	1	0.2350	0.8450	0.3600	-0.0500	0.4700	0.4850
JH0020pax	1	0.0150	1.7550	0.3850	-0.3900	0.5100	1.0550
JH0021pax	1	-1.1000	0.3250	-0.8650	-1.3850	-0.2350	-0.2400
JH0023pax	1	-0.4850	1.2250	0.3900	1.4500	1.0100	1.8450
JH0024pax	1	0.8350	2.0750	0.6950	1.0150	2.8900	2.4000
JH0025pax	1	-0.9850	-0.5650	-0.6350	-1.2100	-0.3500	0.0950
JH0026pax	1	-1.1000	0.7000	0.1500	0.1150	1.3050	1.0750
JH0027pax	1	-3.1650	-2.4400	-2.2300	-1.9300	-2.2400	-1.4900
JH0028pax	1	0.5350	1.3350	1.2450	1.0550	2.8950	1.8900
JH0029pax	1	-1.5700	-0.9750	-0.9300	-1.1200	-0.9200	0.4200
JH0031pax	1	-1.0400	-0.1700	-0.6950	-0.7700	0.0450	0.1250
JH0032pax	1	1.3700	1.6300	0.2650	0.1150	1.7300	1.7250
JH0033pax	1	-1.1900	0.5700	-0.8700	-1.0850	0.9700	-0.5100
JH0034pax	1	-0.7000	0.8150	0.2850	0.1300	1.4900	1.2200
JH0035pax	1	0.0500	1.5700	0.4400	-0.2850	2.1400	1.1050
JH0036pax	1	0.5650	0.9350	0.2450	0.0300	1.7450	0.8500
JH0038pax	1	-0.0100	1.2650	-0.0100	0.0400	1.9650	0.4500
JH0039pax	1	0.2600	0.5550	0.3050	0.8450	3.0050	-0.1900
JH0040pax	1	0.3950	0.9000	0.3650	0.2250	1.1100	0.8850
JH0041pax	1	0.3800	1.2000	-0.0650	-0.3050	1.4900	0.6150
JH0042pax	1	-2.4200	-0.9750	-1.4450	-0.8750	-1.4500	-1.6900
JH0043pax	1	-0.4900	0.3050	0.0001	-0.6800	-0.0800	0.3250
JH0046pax	1	0.2350	0.5950	0.9350	0.0450	1.0300	0.5850
JH0047pax	1	0.3250	2.0950	1.0700	1.4700	1.8200	2.4300
JH0051pax	1	-0.6850	0.2250	-0.1950	-0.8800	-0.0700	-0.1750
JH0052pax	1	-0.4500	0.5050	-0.1700	-0.6150	-0.1350	-0.2700
JH0053pax	1	-1.2800	-0.5550	-0.9600	-0.3500	-0.6500	-0.1450
JH0057pax	1	-0.0450	2.1200	0.3050	0.7500	1.6350	1.4300
JH0059pax	1	-0.5200	0.4200	-0.0500	-0.0650	0.6050	0.5050
JH0060pax	1	-0.7400	0.3250	0.0200	0.2900	0.6600	0.5100
JH0061pax	1	0.9900	2.8050	0.8700	1.4500	3.6400	0.8950
JH0063pax	1	-0.6100	0.5650	-0.2300	-1.0050	0.2750	1.5400
JH0065pax	1	-2.8600	-1.5150	-2.1500	-2.2300	-1.4500	-1.7100

JH0066pax	1	-1.3550	-0.3200	-1.1800	-1.7900	-1.3500	-0.5400
JH0068pax	1	0.0050	0.4550	0.2550	0.0200	1.3500	1.8000
JH0069pax	1	-0.8650	0.2450	-0.2650	-0.5000	-0.0500	-0.6400
JH0071pax	1	-2.5050	-2.2600	-1.8250	-0.3500	-1.3300	-1.5800
JH0072pax	1	0.1100	-0.5750	0.0350	-0.4650	1.3350	0.2300
JH0077pax	1	-0.1000	0.5000	0.4000	0.1150	0.8750	1.7850
JH0078pax	1	1.6350	1.6250	1.6300	0.6600	1.5100	1.7800
JH0080pax	1	-2.3200	-1.2350	-1.2600	-1.0250	-1.5600	0.0450
JH0082pax	1	-0.9000	-0.6650	-0.3200	-0.5450	-0.3550	0.7200
JH0083pax	1	-1.5800	-0.0750	-0.5300	-1.5900	0.2450	0.2050
JH0086pax	1	-0.2250	-0.1850	-0.4800	-1.3250	-0.0850	0.6800
JH0092pax	1	-0.5450	1.3750	0.0400	-0.1050	0.1300	1.1100
MH0001pax	1	1.4250	1.8900	1.5250	1.4350	3.1350	2.2700
MH0009pax	1	-0.2050	0.2150	-0.4850	-0.4450	-0.0400	-0.2050
MH0012pax	1	0.0650	1.3100	0.5700	1.0950	1.4000	1.1200
MH0014pax	1	0.6700	1.1300	0.6100	0.2850	2.6850	1.5750
MH0016pax	1	-1.0950	-0.6050	-0.6750	-1.2050	-0.2450	-0.4300
MH0017pax	1	-0.0100	0.8250	0.2000	-0.4150	1.2500	1.6250
MH0018pax	1	0.9650	0.6700	0.1850	0.2300	2.0650	0.5700
MH0021pax	1	0.9700	0.4800	-0.0650	0.2700	1.9100	1.8700
MH0022pax	1	0.2100	0.7250	0.1150	0.1250	0.8450	1.0950
MH0024pax	1	0.3450	0.6300	0.2050	-0.0550	0.3350	1.0900
MH0028pax	1	0.1350	0.5200	0.1350	-0.5950	0.1250	0.0850
MH0029pax	1	0.2300	0.4850	0.5700	-0.2050	1.3250	0.9050
MH0035pax	1	0.8900	2.2000	1.2200	0.9950	1.3300	1.9450
MH0037pax	1	0.0001	1.3400	0.2600	0.3800	1.5200	2.0000
MH0038pax	1	1.5050	1.4150	1.1650	1.2300	2.1700	1.9850
MH0039pax	1	-1.4900	-0.7350	-0.5400	-0.8300	-0.4350	0.4500
MH0042pax	1	-0.3500	-0.0800	0.0950	-0.2900	-0.1300	0.6500
MH0050pax	1	-1.2600	0.7250	-0.4300	-0.2350	1.1300	1.8350
MH0051pax	1	-1.0300	-0.9000	-0.5750	-1.4350	-1.9200	0.0300
MIP0004pax	1	-2.3200	-2.6150	-1.7200	-1.5500	-1.3550	-2.5350
MP0013Apax	1	0.3150	1.0550	-0.2400	0.0200	1.2450	-0.0700
MP0014Bpax	1	-0.2950	1.1200	-0.1400	0.2950	1.5600	0.3350
MP0018Apax	1	-0.7700	-0.2050	-0.6850	-1.4250	-0.1050	-1.1150
MP0019Bpax	1	-0.9100	-0.5150	-0.7550	-1.0250	-0.6750	0.7300
MP0024pax	1	-1.2900	-0.1150	-0.4700	0.2100	1.3100	0.7400
NK2001pax	1	-0.6250	0.0850	-0.4250	-1.2950	0.1750	1.6050
NK2002pax	1	-0.2400	-0.4300	-0.1450	-0.6550	0.2950	0.7000
NK2003pax	1	-0.4150	0.4150	0.0200	0.0950	1.4100	0.2550
NK2004pax	1	-0.9100	0.3750	-0.6100	-0.8750	0.3500	-0.2700
PB1829pax	1	0.5600	1.7600	0.3700	0.2100	1.8100	1.9150

PB1842pax	1	1.2550	1.6150	1.1550	0.5300	2.5900	1.3450
PB1872pax	1	0.0650	0.3550	0.2400	-0.8650	0.8650	0.0950
PB2857pax	1	-0.8600	0.6800	-0.2350	0.3500	0.0450	1.2500
RC2919pax	1	1.8500	1.8900	1.4100	2.7600	2.8200	3.8300
RC3062pax	1	-0.1750	0.1900	-0.3350	-0.0750	-0.2800	-0.0100
RC3277pax	1	-0.4200	-0.1950	-0.5050	-0.4350	0.3200	-0.0200
RC3297pax	1	0.0600	0.9800	0.1650	0.3850	2.5650	1.0450
RC3445pax	1	-1.0200	-0.4350	-0.6300	-0.9300	0.3100	0.1100
RC3467pax	1	1.9450	2.9300	1.4200	1.2250	2.9400	2.6000

Surprisingly, analysis of the data showed that RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 is present on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 15). The ranges of fold-change in the levels of RNA encoded by these genes normalized to levels of RNA encoded by IL2RB in blood of the training set subjects having colorectal cancer relative to the training set subjects not having any colorectal pathology are shown in Table 15.

Table 15. Sample training set ranges of fold-change in levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene					
	ANXA3	**CLEC4D**	**LMNB1**	**PRRG4**	**TNFAIP 6**	**VNN1**
Average normalized RNA level in subjects having colorectal cancer (ΔCt)	-0.32	0.41	0.78	-0.06	-0.13	0.64
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	0.46	0.99	1.44	0.39	0.65	1.25
Average RNA level fold-change	1.71	1.50	1.58	1.37	1.72	1.53
p-value for average RNA level fold-change	1.1E-08	1.0E-05	8.8E-06	2.3E-06	2.8E-12	6.3E-06
Maximum observed RNA level directional fold-change	12.33	12.20	12.81	6.15	7.38	13.83

As can be seen in Table 15, a test subject having a blood level of RNA encoded by ANXA3, normalized to a level of RNA encoded by IL2RB, which is 1.7 to 12.3 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 15, a test subject having a blood level of RNA encoded by CLEC4D, normalized to a level of RNA encoded by IL2RB, which is 1.5 to 12.2 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 15, a test subject having a blood level of RNA encoded by LMNB1, normalized to a level of RNA encoded by IL2RB, which is 1.6 to 12.8 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 15, a test subject having a blood level of RNA encoded by PRRG4, normalized to a level of RNA encoded by IL2RB, which is 1.4 to 6.2 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 15, a test subject having a blood level of RNA encoded by TNFAIP6, normalized to a level of RNA encoded by IL2RB, which is 1.7 to 7.4 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 15, a test subject having a blood level of RNA encoded by VNN1, normalized to a level of RNA encoded by IL2RB, which is 1.5 to 13.8 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Generation of a logistic regression model (optimized relative to the models set forth in Example 3 of the Examples section, above) for determining the probability that a test subject has colorectal cancer versus not having any colorectal pathology via measurement of levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB: Linear regression analysis of levels of

RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to IL2RB surprisingly showed that a logistic regression model could be generated, based on blood expression levels normalized to IL2RB for the combination of these 6 genes, for discriminating, with a ROC AUC of 0.80, between subjects having colorectal cancer and subjects not having any colorectal pathology (model #191 shown in Table 16).

The model of Table 16 corresponds to:

$P = \{1 + e^{\wedge}-[(0.126) + (-1.406)(L_{ANXA3}) + (0.399)(L_{CLEC4D}) + (1.874)(L_{LMNB1}) + (-1.846)(L_{PRRG4}) + (0.333)(L_{TNFAIP6}) + (-0.277)(L_{VNN1})]\}^{\wedge}-1$,

where P is the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, where L_{ANXA3} is a ratio of a level of RNA encoded by ANXA3 to a level of RNA encoded by IL2RB in blood of the test subject, L_{CLEC4D} is a ratio of a level of RNA encoded by CLEC4D to a level of RNA encoded by IL2RB in blood of the test subject, L_{LMNB1} is a ratio of a level of RNA encoded by LMNB1 to a level of RNA encoded by IL2RB in blood of the test subject, L_{PRRG4} is a ratio of a level of RNA encoded by PRRG4 to a level of RNA encoded by IL2RB in blood of the test subject, $L_{TNFAIP6}$ is a ratio of a level of RNA encoded by TNFAIP6 to a level of RNA encoded by IL2RB in blood of the test subject, and L_{VNN1} is a ratio of a level of RNA encoded by VNN1 to a level of RNA encoded by IL2RB in blood of the test subject.

Table 16. Logistic regression model based on blood expression levels for the combination of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, normalized to IL2RB expression levels for determining the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer. The ROC AUC value for the model is shown for the sample training set used to generate the models, as well as for an independent blind sample test set used to test the model.

Logistic Regression Model #	No. of genes in Model	ROC AUC		Constant (K_0)	Gene-specific regression coefficient (K_n)					
		Training Set	Test Set		ANXA3	CLEC4D	LMNB1	PRRG4	TNFAIP6	VNN1
191	6	0.80	0.80	0.126	-1.406	0.399	1.874	-1.846	0.333	-0.277

Blind sample test set: Quantitative reverse transcriptase-PCR analysis of expression of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 in an independent test set of blood samples from 202 subjects having colorectal cancer and 208 subjects not having any colorectal pathology was performed as described above for the training set (these samples include a subset of the samples listed in Table 12 of Example 3, above, as well as additional samples). The normalized RNA levels measured are shown in Table 17.

Table 17. Sample test set levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 in blood of subjects having colorectal cancer (Group 1) and subjects not having any colorectal pathology (Group 0), normalized to levels of RNA encoded by IL2RB. Levels shown correspond to ΔCt.

Sample ID	**Group**	**Gene**					
		ANXA3	**CLEC4D**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**
PB1952pax	0	2.240	2.125	0.965	2.285	3.220	2.520
RC3142pax	0	2.795	2.380	1.225	2.040	2.675	2.500
CD1728pax	0	2.410	2.330	1.835	2.465	2.345	3.715
PB2015pax	0	2.250	1.835	2.075	3.010	4.220	2.390
PB1786pax	0	1.210	2.530	1.085	2.310	1.555	3.185
CD0762pax	0	1.215	1.260	1.140	2.360	1.925	1.730
CD0800pax	0	2.410	2.310	1.550	2.210	3.480	2.795
PB3267pax	0	1.885	2.565	1.285	2.180	2.325	2.575
PB2267pax	0	2.160	2.890	1.505	2.215	3.085	2.895
CD0411pax	0	2.510	2.950	1.900	2.365	3.890	3.660
CD0211pax	0	1.115	2.235	1.350	2.650	2.470	2.310
PB1918pax	0	2.450	2.080	1.145	1.590	3.675	2.435
PB0701pax	0	1.220	2.090	1.760	2.655	2.190	3.785
PB3445pax	0	1.400	1.870	1.015	1.955	2.280	2.205
PB1763pax	0	2.035	2.435	1.720	2.490	2.975	1.785
PB3213pax	0	2.245	2.340	1.390	1.795	2.255	2.100
CD1424pax	0	1.460	1.300	1.220	1.975	2.535	2.510
PB2978pax	0	2.945	3.175	1.990	2.175	3.680	2.840
PB3270pax	0	1.895	3.055	0.885	1.415	1.280	2.545
RC2030pax	0	1.580	2.060	1.205	1.595	1.665	4.080
CD0448pax	0	2.195	2.955	1.800	2.400	4.090	3.800
RC2869pax	0	1.620	1.415	0.880	1.475	2.500	2.520

PB4296pax	0	1.940	2.600	1.445	1.765	2.290	3.890
CD0398pax	0	2.425	2.560	1.970	2.265	4.015	3.515
CD1077pax	0	0.740	0.845	0.575	1.560	1.410	1.560
PB3805pax	0	2.040	1.655	1.515	1.605	1.020	1.610
PB1898pax	0	2.075	2.445	1.180	1.800	3.165	1.410
PB2062pax	0	2.090	2.110	1.455	1.850	3.090	2.220
CD0937pax	0	1.120	0.705	0.655	1.365	2.310	1.860
RC2612pax	0	2.725	2.685	1.810	1.830	3.395	2.535
CD1784pax	0	1.615	1.410	1.325	1.735	2.325	2.325
PB2984pax	0	1.205	2.325	0.990	1.895	2.270	2.315
RC2976pax	0	-0.045	1.445	-0.305	0.685	-0.305	3.570
PB1785pax	0	1.470	1.950	1.245	1.880	1.835	1.450
CD0691pax	0	1.785	2.850	1.445	2.060	2.535	1.900
PB2384pax	0	1.700	2.440	0.915	1.380	2.500	2.405
CD1550pax	0	2.420	3.640	2.150	2.235	3.065	3.690
CD1540pax	0	1.005	0.905	0.785	1.465	1.745	0.990
RC2565pax	0	-0.125	0.690	-0.330	0.735	0.200	1.790
CD0499pax	0	1.390	2.750	0.805	1.720	2.820	1.290
RC2174pax	0	0.440	1.020	0.790	1.700	1.705	2.265
PB3304pax	0	0.550	1.270	0.520	1.760	2.765	0.835
PB1879pax	0	1.345	1.065	1.295	1.620	2.070	1.830
PB3808pax	0	1.450	1.405	1.225	1.580	2.810	2.435
PB4357pax	0	1.065	0.195	0.295	0.690	1.245	0.360
PB2636pax	0	1.795	2.615	1.360	1.775	3.600	2.925
PB3440pax	0	1.320	1.720	1.280	1.515	0.640	1.495
PB2272pax	0	2.225	2.130	1.335	1.475	3.785	1.805
PB1848pax	0	1.410	1.150	0.765	0.875	2.300	2.775
RC3420pax	0	1.265	1.490	1.390	2.060	2.875	0.995
PB2005pax	0	1.800	1.830	1.045	1.285	3.465	2.250
CD0354pax	0	0.680	1.160	0.585	1.395	2.015	1.265
CD1945pax	0	1.005	1.500	0.260	0.815	2.430	2.055
PB4156pax	0	2.005	2.405	1.435	1.370	1.995	1.990
RC2934pax	0	1.055	1.185	0.605	1.025	2.760	2.560
PB2214pax	0	1.350	1.790	0.535	0.980	2.390	1.315
PB3370pax	0	0.965	2.430	1.125	1.795	1.985	2.235
PB1300-2pax	0	0.885	1.535	0.425	0.960	1.765	1.860
PB2951pax	0	-0.180	-1.980	-1.215	-0.650	-0.520	-0.915
PB3356pax	0	-0.430	1.050	-0.145	1.105	0.680	1.550
CD0148pax	0	0.740	1.890	0.515	1.255	1.835	1.665
PB3451pax	0	1.240	1.300	0.720	1.025	2.210	1.555
CD1409pax	0	0.510	0.115	0.140	0.495	0.660	1.250
PB3118pax	0	1.480	1.615	1.415	1.375	1.195	1.855

PB3931pax	0	1.460	1.515	0.925	1.250	2.790	1.210
CD1163pax	0	1.105	2.110	1.475	2.175	3.175	1.875
RC2112pax	0	1.255	2.285	1.555	1.830	1.825	2.530
PB4274pax	0	0.670	0.385	0.075	0.245	0.535	1.735
CD1028pax	0	1.250	2.115	0.985	1.370	2.240	1.950
PB4345pax	0	0.680	1.445	0.895	1.320	1.125	2.145
CD0698pax	0	0.925	1.555	0.915	1.295	1.265	1.515
PB4066pax	0	0.855	0.175	0.580	0.940	1.450	0.185
PB4062pax	0	0.720	1.380	0.455	1.305	2.385	0.300
PB3481pax	0	-0.110	0.835	0.185	1.025	0.445	1.345
CD0252pax	0	1.100	0.340	0.380	0.615	2.185	0.580
CD0428pax	0	0.480	1.090	0.225	0.815	1.420	1.465
CD0571pax	0	1.060	1.425	1.430	1.960	2.575	0.890
CD0786pax	0	0.850	1.335	0.795	1.290	2.045	1.325
PB3863pax	0	1.745	1.785	1.435	1.255	2.620	2.605
PB2927pax	0	1.955	0.820	0.520	-0.140	1.515	1.890
PB3568pax	0	1.505	1.625	1.250	1.295	2.155	1.370
RC2839pax	0	0.690	1.275	0.595	0.935	1.195	1.800
CD1700pax	0	1.095	1.520	1.160	1.250	1.480	2.020
CD1313pax	0	1.600	1.400	0.710	0.820	2.670	0.510
PB1700pax	0	0.690	1.020	0.740	1.155	1.610	1.265
CD0727pax	0	1.515	2.780	1.015	1.245	2.130	1.450
PB4161pax	0	0.940	0.945	0.755	0.890	1.340	1.330
CD1583pax	0	0.690	0.855	0.530	0.780	1.240	1.445
PB3594pax	0	0.885	1.175	0.500	0.935	2.395	1.040
RC3170pax	0	0.860	1.635	0.190	0.210	0.400	2.110
CD0553pax	0	2.075	3.365	1.750	1.505	2.725	3.125
CD0220pax	0	1.080	2.120	1.110	1.210	1.380	2.345
CD0238pax	0	0.355	1.010	0.440	1.065	1.720	1.180
CD0409pax	0	-0.235	0.710	-0.100	0.650	0.505	1.320
PB3163pax	0	0.530	1.630	0.885	1.515	2.675	2.245
PB2491pax	0	0.835	-0.035	0.295	0.605	2.505	0.150
PB4377pax	0	0.110	0.315	0.030	0.565	1.245	1.270
PB4307pax	0	1.845	3.790	1.730	1.775	3.650	3.665
RC2236pax	0	0.970	1.080	1.035	0.985	1.450	2.095
RC2716pax	0	0.490	0.730	0.845	1.360	2.490	1.365
PB2024pax	0	0.815	1.375	0.785	1.075	2.445	1.850
CD0484pax	0	0.140	1.135	0.255	1.080	1.585	0.255
RC2897pax	0	0.385	1.035	0.130	0.530	1.350	1.335
CD0872pax	0	0.580	-0.005	0.490	0.585	1.435	1.005
PB1626pax	0	0.525	0.835	0.435	0.550	1.075	1.865
CD1974pax	0	0.965	1.445	0.350	0.555	2.000	0.985

CD1295pax	0	0.560	0.450	0.425	0.560	1.575	1.570
RC2699pax	0	0.825	1.015	0.340	0.395	1.385	1.285
RC2986pax	0	1.095	1.315	0.540	0.625	2.675	1.710
PB1899pax	0	-0.230	0.420	-0.365	0.095	0.270	1.625
PB3955pax	0	1.630	1.745	1.220	1.070	3.000	1.545
PB1230pax	0	0.685	1.585	0.855	0.955	0.950	1.870
CD1404pax	0	-0.045	1.190	0.225	0.740	1.330	2.630
CD0367pax	0	1.050	0.940	0.745	0.705	2.105	1.360
PB3226pax	0	0.720	1.225	0.760	1.010	2.320	1.735
PB3193pax	0	0.475	0.650	0.650	0.905	1.600	1.205
PB3224pax	0	0.400	-0.115	0.080	0.125	0.415	0.390
PB1871pax	0	0.715	0.640	0.565	0.545	1.590	1.710
CD1392pax	0	1.055	1.540	0.860	1.030	2.995	1.720
CD0833pax	0	-0.050	-0.365	-0.090	0.365	0.630	-0.285
CD0386pax	0	1.070	2.390	1.000	1.280	3.245	2.350
CD1158pax	0	0.335	0.270	0.110	0.065	0.185	1.405
PB1324pax	0	-0.110	0.585	0.465	1.050	1.765	1.840
CD1455pax	0	-0.610	0.530	0.345	1.150	0.755	1.570
RC2338pax	0	1.395	2.355	1.590	1.460	2.515	2.445
CD1971pax	0	0.645	1.425	0.060	0.110	1.400	2.170
CD1048pax	0	0.860	2.110	1.115	1.525	2.600	1.210
CD0244pax	0	0.285	0.305	0.260	0.670	1.395	-0.095
RC3191pax	0	1.560	2.415	1.510	1.210	2.285	2.395
PB3582pax	0	1.090	1.830	1.230	1.320	2.870	1.955
CD0237pax	0	0.595	1.085	0.245	0.400	1.400	0.985
CD1981pax	0	1.955	3.135	1.875	1.495	3.520	3.250
CD0603pax	0	1.015	1.015	0.640	0.400	1.755	1.770
CD1134pax	0	0.795	1.655	0.815	0.790	1.850	2.475
PB2130pax	0	0.665	0.890	0.335	0.260	0.895	1.155
PB1275pax	0	-0.885	0.195	-0.445	0.145	-0.230	2.010
PB2564pax	0	0.385	1.960	0.460	0.810	1.055	1.265
CD0580pax	0	1.150	1.580	0.470	0.400	2.330	1.165
PB0768pax	0	-0.670	0.740	0.080	0.825	0.425	1.335
CD0518pax	0	1.575	3.770	1.750	1.775	3.120	2.440
RC3315pax	0	0.640	1.565	0.650	1.035	2.680	0.940
CD1270pax	0	0.895	1.020	0.770	0.515	1.695	1.680
CD1068pax	0	0.380	0.200	0.700	0.985	2.475	0.400
CD0995pax	0	0.805	1.465	0.560	0.615	2.395	1.435
CD1438pax	0	-0.125	0.620	-0.030	0.440	0.905	0.045
CD1169pax	0	0.270	0.295	0.470	0.500	1.845	1.430
RC3379pax	0	0.850	1.185	0.460	0.410	1.945	0.400
CD0520pax	0	-0.125	1.025	0.990	1.325	1.130	1.370

PB1718pax	0	0.145	1.185	0.395	0.445	0.695	1.505
PB2757pax	0	0.555	1.690	0.995	0.915	1.750	2.335
CD0743pax	0	0.290	-0.400	0.095	0.070	1.515	-0.120
CD0667pax	0	-0.385	-0.305	-0.345	-0.065	0.205	-0.230
RC3214pax	0	0.940	1.860	1.200	1.140	2.730	1.620
PB0689pax	0	0.235	1.420	0.295	0.270	0.905	1.990
CD0911pax	0	-0.550	-0.580	-0.800	-0.405	0.290	-0.560
PB2516pax	0	0.310	1.075	0.700	0.490	0.890	2.285
PB2584pax	0	0.945	1.230	0.935	0.475	1.270	1.340
CD1487pax	0	0.310	2.120	1.190	1.645	2.160	0.815
CD0282pax	0	0.165	0.685	0.270	0.545	1.100	-0.700
PB4325pax	0	0.065	-0.180	-0.020	-0.025	0.475	-0.360
RC2652pax	0	-1.425	0.025	-0.620	0.450	0.760	0.560
PB2464pax	0	0.620	1.330	0.510	0.045	1.230	2.810
PB3227pax	0	0.235	0.850	0.820	0.865	2.215	1.845
CD1559pax	0	0.170	1.000	0.335	0.505	2.070	1.300
PB4003pax	0	0.070	0.655	0.170	0.215	0.880	0.690
CD0108pax	0	0.260	0.055	0.560	0.310	0.740	0.640
PB1758pax	0	-0.600	0.475	0.030	0.535	0.500	0.145
CD0277pax	0	0.605	1.980	0.800	0.940	2.250	0.720
PB2184pax	0	-1.005	-0.650	-0.705	-0.445	-0.075	1.230
CD1683pax	0	0.485	1.620	0.725	0.575	1.595	1.805
RC2615pax	0	-0.655	0.070	0.210	0.340	0.190	1.205
CD1224pax	0	-0.295	0.630	-0.325	-0.110	0.995	0.485
CD1458pax	0	0.035	-0.055	0.560	0.485	1.635	0.585
CD0204pax	0	0.380	0.885	0.250	-0.050	1.200	0.990
CD1706pax	0	0.540	1.815	1.025	1.020	2.510	1.195
CD1542pax	0	0.375	0.870	0.900	0.655	1.755	1.305
PB2909pax	0	-0.345	-1.240	-0.675	-0.915	-0.075	-0.645
PB4073pax	0	-0.250	0.195	-0.095	-0.205	0.410	0.600
CD0604pax	0	0.415	1.130	0.320	0.235	2.125	0.230
PB3605pax	0	-1.120	-0.290	-0.695	-0.340	0.305	0.660
CD1965pax	0	0.030	1.310	0.400	0.140	1.155	2.275
CD0432pax	0	0.185	0.565	0.015	-0.140	1.870	0.495
PB1336pax	0	0.695	0.780	0.320	-0.470	1.310	1.805
PB2974pax	0	-0.635	0.320	-0.300	-0.305	0.605	1.740
PB0662pax	0	0.120	0.575	0.945	0.850	1.605	0.045
CD1741pax	0	-0.310	-0.335	0.015	-0.160	1.205	0.850
PB2875pax	0	-0.230	1.205	0.140	0.165	1.200	1.025
CD0419pax	0	0.440	1.220	0.810	0.655	2.375	-0.030
CD1649pax	0	0.925	1.565	1.000	0.130	1.550	1.630
CD1329pax	0	0.130	-0.170	0.155	-0.460	1.075	0.705

CD0466pax	0	0.730	1.870	0.930	0.160	1.280	1.890
CD0857pax	0	-1.460	-0.755	-0.560	-0.360	-0.670	0.255
CD0242pax	0	0.965	1.360	0.580	-0.450	0.980	1.235
PB3513pax	0	-0.355	-0.705	-0.970	-1.200	0.410	-1.270
CD0583pax	0	-0.605	-1.045	-0.595	-0.740	0.765	-0.705
PB3049pax	0	-1.030	0.045	-0.235	-0.170	0.105	0.595
PB1446pax	0	-1.380	-0.485	-0.715	-0.495	0.300	0.700
CD1441pax	0	-0.565	0.485	0.230	0.175	0.995	0.055
PB2634pax	0	0.165	1.335	1.270	1.000	2.740	1.020
CD0547pax	0	-1.740	-0.260	-0.685	-0.185	-0.095	-0.420
PB2041pax	0	-0.655	0.440	-0.205	-0.170	1.540	0.185
PB1514pax	0	-0.940	0.075	-0.280	-0.265	0.850	0.175
PB3032pax	0	-0.145	0.435	0.750	0.110	1.510	1.425
CD0676pax	0	-0.730	-0.640	-0.610	-1.085	0.300	0.100
PB3806pax	0	-1.410	0.325	-0.305	-0.080	-0.010	-0.070
CD0472pax	0	-1.800	-0.180	-0.830	-0.465	0.255	-0.070
PB1222pax	0	-0.165	0.415	0.325	-0.795	-0.035	0.860
CD1032pax	0	-2.740	-2.045	-0.550	-0.490	-0.875	0.410
JH0111pax	1	1.040	1.910	0.835	2.170	2.645	1.650
MH0122Bpax	1	0.235	1.190	0.340	1.380	0.430	3.590
IS3001pax	1	1.925	2.145	1.030	1.300	1.885	2.880
BE3003pax	1	0.985	1.160	1.050	1.985	2.185	1.120
MH0083pax	1	1.570	1.635	0.805	1.195	2.150	1.765
BE1004pax	1	0.085	1.050	0.730	1.825	2.040	1.790
MH0112Bpax	1	0.960	1.720	0.810	1.325	1.975	2.055
BE1007pax	1	1.050	0.945	0.815	1.055	1.810	2.100
MH0031-2pax	1	-0.325	-0.130	-0.430	0.615	1.330	1.170
MH0112Apax	1	0.925	1.760	1.025	1.500	2.025	2.220
MR4001Apax	1	0.610	1.130	0.470	1.210	1.650	0.615
NK2011pax	1	1.355	2.025	1.060	1.110	2.520	3.570
OL0092pax	1	0.790	1.555	0.670	1.160	1.585	1.650
MIP2007pax	1	1.075	1.725	0.855	1.265	2.410	1.980
JH0153pax	1	1.085	1.470	0.610	0.580	0.495	2.085
KW0005pax	1	0.695	1.540	1.240	1.940	2.705	1.850
JH0054pax	1	0.555	1.775	0.870	1.580	1.990	1.710
AN4017pax	1	1.190	1.630	0.590	0.510	0.620	1.665
MP0031Apax	1	1.090	1.315	0.705	0.800	1.720	1.570
MP0021Bpax	1	0.410	0.995	0.710	1.220	1.765	1.555
MIP1018Bpax	1	0.600	1.535	0.490	1.020	1.720	1.115
CC0005pax	1	0.655	0.940	0.345	0.725	1.460	0.345
NK1009pax	1	1.915	1.845	1.030	0.650	2.595	1.635
JM0010pax	1	0.130	0.610	0.670	1.075	1.260	1.775

JH0150pax	1	0.895	1.930	0.490	0.685	0.900	0.730
IS1004pax	1	1.495	2.710	1.750	1.520	2.570	3.730
MIP1021Bpax	1	0.600	2.605	0.860	1.455	2.305	2.180
NK5006pax	1	0.895	1.205	0.645	0.620	2.095	2.495
MP0032Bpax	1	0.630	1.060	0.315	0.640	1.770	0.865
BE3012Apax	1	-0.830	-0.545	-1.045	-0.330	-0.330	0.700
JH0146pax	1	-0.130	0.615	0.175	0.805	1.540	1.665
NK2007pax	1	0.110	0.520	-0.030	0.560	0.980	-0.125
JH0112pax	1	0.500	0.910	0.265	0.530	1.635	1.090
OL0066pax	1	0.140	1.050	0.380	0.785	1.140	1.410
DC0012pax	1	-1.370	-0.520	-0.775	0.275	-1.140	-0.350
JH0129pax	1	0.580	1.530	0.935	1.265	2.850	2.270
JH0163pax	1	0.295	1.490	0.955	1.580	2.625	1.310
FS0005pax	1	0.040	0.315	0.500	0.890	1.355	0.850
DES1006Apax	1	0.955	1.140	0.890	0.635	1.570	1.940
MH0030pax	1	-0.150	0.865	0.180	0.720	0.345	0.260
FS0006pax	1	0.100	0.195	0.585	0.825	1.165	1.025
OL0096pax	1	0.305	1.230	0.890	0.830	0.405	2.550
MIP2003pax	1	-0.045	0.665	0.295	0.835	1.865	1.060
MH0113Apax	1	0.495	0.085	0.800	0.575	1.015	1.565
JH0067pax	1	0.230	0.940	0.100	0.355	1.180	0.980
MH0053pax	1	2.195	2.465	1.420	0.670	3.315	2.550
MW0001Apax	1	0.345	1.160	0.540	0.680	1.290	1.545
AN4013pax	1	1.135	2.150	1.055	0.770	1.810	2.225
WJ0005CSpax	1	-0.895	-0.630	-1.440	-0.840	0.055	0.250
JH0096pax	1	-1.745	-0.480	-1.130	-0.400	-2.050	1.375
DC5008Bpax	1	0.045	0.855	0.140	0.300	1.415	2.280
MIP2002pax	1	1.120	1.680	1.060	0.755	2.000	1.890
AN0011pax	1	1.110	1.075	0.125	-0.780	0.320	2.935
DES1009Apax	1	0.305	0.660	0.325	0.440	0.955	0.370
DC0011pax	1	0.150	0.700	0.615	0.730	1.535	1.880
FC0013pax	1	-0.105	-0.095	0.920	0.965	1.255	2.145
OL0075pax	1	-0.590	0.190	-0.010	0.590	1.140	0.970
NK2014pax	1	0.485	1.240	0.650	0.745	1.705	1.100
KW0008pax	1	0.090	0.985	0.305	0.250	0.220	1.730
OL0080pax	1	-0.445	-0.025	-0.150	0.110	0.030	0.540
AN4019pax	1	1.520	2.265	1.045	0.765	3.090	1.225
JH0116pax	1	0.035	1.465	0.520	0.830	1.040	1.120
JH0132pax	1	-0.460	0.010	-0.310	0.095	0.365	-0.005
JH0170pax	1	2.050	2.960	1.645	0.855	3.655	3.370
NK1001pax	1	0.415	0.990	-0.050	-0.025	1.805	0.975
OL0065pax	1	0.280	0.730	0.445	0.530	1.630	0.690

BE3011Apax	1	0.640	1.825	0.600	0.680	2.150	1.105
KW0004pax	1	0.895	2.485	1.415	1.290	1.975	1.935
JH0022pax	1	-0.265	0.255	0.040	0.145	0.375	0.945
JH0100pax	1	0.550	1.420	1.020	0.955	1.955	1.405
CD1690pax	1	0.120	0.145	0.110	0.165	1.040	-0.315
MH0063pax	1	0.265	-0.295	-0.305	-0.215	2.185	-0.590
MIP1017pax	1	-0.260	0.825	-0.250	0.000	0.670	0.800
JH0109pax	1	1.190	2.160	1.000	0.405	2.055	2.640
CC0001pax	1	0.170	0.765	0.295	0.315	1.785	1.305
PB3545pax	1	-0.520	1.150	-0.380	0.170	0.795	0.475
IS4001pax	1	-0.855	-0.065	-0.915	-0.770	-0.370	1.630
DC0005pax	1	1.085	1.960	1.220	0.715	1.895	1.965
MH0070pax	1	0.380	0.945	0.685	0.515	1.575	1.395
JH0114pax	1	-1.875	-1.485	-1.400	-0.540	-1.710	-1.970
CD1351pax	1	0.510	0.515	0.015	-0.295	1.830	0.785
OL0093pax	1	-2.055	-0.120	-1.075	0.025	-0.430	0.560
JH0058pax	1	-0.610	0.305	0.165	0.240	-0.060	1.195
DC5008Apax	1	-0.395	0.160	-0.190	-0.155	1.135	1.540
OL0085pax	1	-0.985	-0.050	-0.750	-0.290	0.505	0.520
FS1022pax	1	-0.530	0.295	0.400	0.675	0.655	0.040
OL0063pax	1	-0.915	-0.430	-0.335	-0.025	0.055	-0.085
MH0108Apax	1	0.215	0.810	0.225	-0.005	0.885	0.570
MIP2006pax	1	-0.590	0.470	-0.025	0.265	0.505	0.080
NK2016pax	1	-0.220	0.425	0.075	0.215	1.975	0.835
OL0057pax	1	-0.975	-0.970	-1.340	-1.210	-0.630	-0.575
JH0137pax	1	0.265	1.395	0.095	-0.125	1.190	1.175
JH0118pax	1	0.030	-0.565	0.010	-0.405	0.610	0.125
MH0097pax	1	-0.785	-0.180	-0.195	-0.015	0.345	0.430
JH0147pax	1	0.770	2.080	0.915	0.855	3.475	1.255
BE4002pax	1	0.160	0.420	0.015	-0.445	0.760	1.265
MH0036pax	1	-0.090	0.620	0.370	0.240	1.430	1.440
JH0142pax	1	-0.585	0.220	-0.185	0.055	0.285	-0.605
MIP2010Apax	1	0.285	0.555	-0.075	-0.280	1.550	-0.070
JH0169pax	1	-0.305	0.255	-0.120	-0.320	0.455	1.110
FS1010pax	1	0.435	1.705	1.210	0.800	1.520	2.145
JGA0036pax	1	-0.515	0.390	-0.595	-0.995	-0.725	2.090
MH0079pax	1	0.395	0.625	0.275	-0.375	0.500	1.020
OL0064pax	1	0.030	0.500	0.305	0.120	1.345	0.580
JH0135pax	1	-1.480	-1.890	-1.505	-1.320	-1.655	-1.480
OL0017pax	1	-0.790	-0.650	-0.375	-0.315	0.900	0.765
CC2001pax	1	-0.285	1.450	0.335	0.480	1.315	1.210
DC6002Apax	1	-0.570	0.975	0.200	0.395	0.930	1.000

JH0149pax	1	0.485	1.165	0.240	-0.065	2.395	0.980
DC2009pax	1	-0.715	0.050	0.195	0.155	-0.350	0.365
MP0033Bpax	1	0.145	1.045	0.320	0.075	1.285	0.715
MP0030Bpax	1	-0.875	0.445	0.270	0.690	2.285	1.790
JH0133pax	1	-0.335	0.500	0.045	-0.220	0.210	1.150
OL0059pax	1	-1.335	-0.180	-0.735	-0.290	-0.065	-0.145
AN4026Bpax	1	-0.175	0.485	0.215	-0.160	0.510	1.130
AN4022Apax	1	-0.540	0.830	-0.290	-0.355	0.020	0.710
OL0077pax	1	-1.055	-0.525	-0.085	0.035	0.200	0.165
OL0094pax	1	-0.305	0.535	0.190	0.015	0.710	0.460
KW0002pax	1	-0.625	0.165	-0.505	-0.695	0.470	1.215
MH0066pax	1	-1.180	-0.855	-0.710	-0.595	-0.320	-0.480
DC5006Apax	1	-0.210	0.160	0.105	-0.385	-0.220	0.280
NK4001pax	1	-0.975	1.135	-0.090	0.260	0.500	0.810
JGA0029pax	1	-0.870	0.590	-0.575	-0.195	1.295	0.185
MW0008Apax	1	-1.080	-0.505	-0.480	-0.440	-0.300	-0.285
JH0131pax	1	-0.640	-0.890	-0.935	-1.555	-1.150	0.180
JH0106pax	1	-0.720	-0.200	-0.105	-0.290	0.845	1.115
OL0056pax	1	-0.495	-1.310	-0.470	-0.925	1.175	0.450
MH0076pax	1	0.515	1.955	0.540	-0.075	2.340	2.570
NK2005pax	1	-1.575	-1.090	-0.925	-1.055	-2.160	-0.020
MP0029Apax	1	-1.700	-0.870	-1.100	-0.670	0.275	0.060
MH0080pax	1	-0.310	0.215	0.340	0.120	1.530	0.510
FS1014pax	1	-0.580	0.050	-0.030	0.045	1.850	-0.105
JH0110pax	1	-0.565	0.185	-0.375	-0.830	-0.420	0.735
JH0145pax	1	-2.030	-0.365	-0.940	-0.500	-1.170	0.445
MH0125Apax	1	-0.550	1.265	0.135	-0.170	0.465	2.310
OL0058pax	1	-0.935	-1.050	-0.840	-0.870	0.115	-1.495
DC0008pax	1	0.545	0.990	0.665	-0.070	1.875	0.815
MH0073pax	1	-1.290	-0.595	-1.165	-1.040	0.040	-0.285
MIP0002pax	1	-2.285	-0.925	-1.240	-0.595	-0.575	0.055
JH0138pax	1	-0.680	0.150	-0.065	-0.315	0.120	0.340
OL0074pax	1	-1.255	-0.530	-0.680	-0.410	1.280	0.145
OL0079pax	1	-0.920	-0.125	-0.510	-0.755	-0.360	0.460
MR1001pax	1	-0.120	0.795	0.015	-0.490	0.650	0.495
DES5001Bpax	1	-1.335	0.395	-1.095	-0.735	0.770	0.315
MH0093pax	1	-2.215	-1.375	-1.240	-0.880	-0.800	0.255
MP0027Apax	1	-0.415	0.765	-0.140	-0.350	0.940	0.200
IS1005Apax	1	-1.180	-1.030	-0.340	-0.445	0.325	-0.025
KW0003pax	1	-0.295	0.830	0.335	-0.580	-0.325	2.740
CD1260pax	1	-0.730	-1.005	-0.325	-0.795	0.725	0.510
JH0130pax	1	-1.110	-0.400	-0.940	-1.210	-0.505	0.220

MH0096pax	1	-1.225	0.790	-0.670	-0.420	0.865	0.665
OL0052pax	1	-1.075	-1.005	-0.060	-0.315	0.040	-0.265
MIP0005pax	1	-2.020	-1.140	-1.305	-0.835	-0.420	-1.190
OL0014pax	1	-2.000	-2.250	-1.480	-1.640	-1.645	-0.705
WJ0003RTpax	1	-1.935	-1.860	-1.760	-1.735	-1.070	-1.055
MIP2013Bpax	1	0.025	1.825	0.110	-0.890	-0.500	1.975
JH0164pax	1	-0.115	0.335	0.015	-0.615	1.275	0.005
JH0123pax	1	-2.050	-1.365	-1.125	-0.920	-1.165	-1.315
OL0089pax	1	-1.415	0.130	-0.455	-0.365	-0.305	-0.520
DES1013Bpax	1	-1.130	0.105	-0.450	-0.595	0.160	0.065
AN4011pax	1	-0.155	0.805	0.770	0.280	2.110	0.880
JH0093pax	1	0.095	1.090	0.085	-0.695	1.290	0.885
OL0043pax	1	-0.705	-0.475	-0.555	-1.105	0.230	-0.335
JH0097pax	1	-0.280	-0.285	0.270	-0.445	0.780	-0.415
DC3003pax	1	-0.265	0.975	0.030	-0.625	1.600	1.845
OL0068pax	1	-1.790	-0.720	-1.340	-1.230	-0.665	-0.895
KW0006pax	1	-1.320	0.575	0.155	0.080	0.700	1.540
NK5008pax	1	-1.150	-1.435	-1.000	-1.300	0.610	-1.040
DC6001Apax	1	-0.965	0.725	-0.225	-0.670	0.135	1.500
OL0034pax	1	-1.155	-0.515	-0.985	-1.375	0.485	0.545
MH0062pax	1	-1.040	-0.245	-0.205	-0.600	0.450	0.300
MIP1019Apax	1	-1.415	-0.495	-1.060	-1.125	0.800	-0.060
MR1002pax	1	-0.890	0.295	0.315	-0.070	0.645	0.355
MH0090pax	1	-0.995	0.240	-0.365	-0.705	0.000	-0.495
NK2010pax	1	-1.505	-1.070	-0.985	-1.320	-0.870	-1.045
NK2009pax	1	0.060	0.745	0.470	-0.370	1.920	0.300
NK2018pax	1	-2.160	-1.415	-1.155	-1.090	-0.640	-1.100
JH0144pax	1	0.475	2.560	1.160	0.215	2.295	1.575
OL0078pax	1	-2.540	-2.250	-1.570	-1.555	-1.350	-1.325
MIP1009pax	1	-2.950	-1.590	-2.030	-1.500	-0.685	-1.165
OL0025pax	1	-2.010	-0.060	-0.940	-0.855	-0.380	-0.445
MH0078pax	1	-0.910	0.290	-0.405	-1.410	-0.335	1.345
KW0007pax	1	-0.655	0.930	0.090	-0.640	0.830	0.495
AN0013pax	1	0.060	1.905	0.875	-0.085	2.740	2.020
JH0076pax	1	-0.535	-0.795	-0.360	-1.735	-0.300	-0.065
OL0090pax	1	-1.105	0.150	0.090	-0.745	0.075	0.990
JH0120pax	1	-0.040	0.595	0.215	-0.935	1.860	0.390
JH0126pax	1	-1.570	-0.110	-0.455	-1.020	-0.435	0.415
JH0113pax	1	-0.055	0.805	0.605	-0.715	0.835	0.570
JH0085pax	1	-0.960	-0.445	-0.075	-1.095	0.185	0.295
MH0081pax	1	0.390	1.375	0.640	-0.845	2.085	1.300
AN0001pax	1	-1.830	-1.010	-0.840	-1.320	0.110	-0.175

MH0095pax	1	-2.145	-1.475	-1.350	-1.795	-0.915	-0.830
DS0007pax	1	-3.365	-2.210	-1.965	-1.820	-3.555	-2.965
JH0136pax	1	-2.355	-1.670	-0.970	-1.215	-0.845	-1.710
OL0072pax	1	-1.135	-0.315	-0.375	-1.170	0.415	-0.875
BE1006pax	1	-2.635	-1.570	-1.580	-1.735	-0.580	-0.740
JH0048pax	1	-2.285	-0.250	-1.315	-1.350	-1.075	-2.025
OL0073pax	1	-2.980	-2.425	-1.650	-1.685	-0.100	-0.650
FS0002pax	1	-2.275	-1.035	-0.730	-1.030	-0.780	-1.700
OL0041pax	1	-1.890	-1.030	-1.595	-2.325	-0.970	-1.465
AN0007pax	1	-3.105	-1.775	-2.300	-3.180	-2.690	-1.255

The test set results confirmed the surprising finding based on the training set that ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 each express RNA on average at a significantly higher level (p-value less than 0.05) in blood of subjects having colorectal cancer relative to subjects having no colorectal pathology (Table 18). The ranges of fold-change in the levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of the test set subjects having colorectal cancer relative to the test set subjects not having any colorectal pathology are also shown in Table 18.

Table 18. Sample test set ranges of fold-changes in levels of RNA encoded by ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to levels of RNA encoded by IL2RB in blood of subjects having colorectal cancer relative to subjects not having any colorectal pathology.

	Gene					
	ANXA3	**CLEC4D**	**LMNB1**	**PRRG4**	**TNFAIP6**	**VNN1**
Average normalized RNA level in subjects having colorectal cancer (ΔCt)	-0.37	0.39	-0.04	-0.07	0.76	0.74
Average normalized RNA level in subjects not having any colorectal pathology (ΔCt)	0.72	1.21	0.65	0.90	1.73	1.51
Average RNA level fold-change	2.12	1.77	1.61	1.97	1.95	1.70
p-value for average RNA level fold-change	2.8E-24	3.0E-14	3.3E-19	1.9E-26	5.0E-17	2.4E-12
Maximum observed RNA level directional fold-change	16.95	12.44	7.71	16.96	38.96	22.19

As can be seen in Table 18, a test subject having a blood level of RNA encoded by ANXA3, normalized to a level of RNA encoded by IL2RB, which is 2.1 to 17.0 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 18, a test subject having a blood level of RNA encoded by CLEC4D, normalized to a level of RNA encoded by IL2RB, which is 1.8 to 12.4 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 18, a test subject having a blood level of RNA encoded by LMNB1, normalized to a level of RNA encoded by IL2RB, which is 1.6 to 7.7 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 18, a test subject having a blood level of RNA encoded by PRRG4, normalized to a level of RNA encoded by IL2RB, which is 2.0 to 17.0 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 18, a test subject having a blood level of RNA encoded by TNFAIP6, normalized to a level of RNA encoded by IL2RB, which is 2.0 to 39.0 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

As can be seen in Table 18, a test subject having a blood level of RNA encoded by VNN1, normalized to a level of RNA encoded by IL2RB, which is 1.7 to 22.2 fold higher than the average level of RNA encoded by this gene in blood of subjects not having any colorectal pathology is more likely to have colorectal cancer than to not have any colorectal pathology.

Furthermore, the test set results confirmed the surprising finding based on the training set that logistic regression model #191 based on blood expression levels of the combination of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, each of which normalized against expression levels of IL2RB, can be used to discriminate, with a ROC AUC of at least 0.80 (Table 16), between subjects having colorectal cancer and subjects not having any colorectal pathology. As such, the novel logistic regression model #191 can be used to determine the probability that a test subject has colorectal cancer as opposed to not having any colorectal pathology, based on blood levels of expression of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and/or VNN1 normalized to those of IL2RB.

EXAMPLE 7

Determination of the probability that a test subject has colorectal cancer as opposed to not having colorectal cancer using blood levels of RNA encoded by the colorectal cancer markers: ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 normalized to those of IL2RB.

A blood sample from a test subject is analyzed for levels of RNA encoded by ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1 as described in Example 1, above, thereby generating test data. Logistic regression model #191 of Table 16 is applied to the test data, thereby providing the probability that the test subject has colorectal cancer as opposed to not having any colorectal pathology.

All patents, patent applications, and published references cited herein are hereby incorporated by reference in their entirety.

One skilled in the art will appreciate readily that the invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those objects, ends and advantages inherent herein. The present examples, along with the methods, procedures, treatments, molecules, and specific compounds described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention as defined by the scope of the claims.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.

WHAT IS CLAIMED IS:

1. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:
(a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data;
(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and
(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,
wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.
2. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:
(a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data;
(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and
(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,
wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

3. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:
(a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject,

thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

4. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

5. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

6. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

7. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

8. The method of claim 1, 2, 3, 4, 5, 6 or 7, wherein the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject.

9. The method of claim 1, 2, 3, 4, 5, 6 or 7, further comprising determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer.

10. The method of claim 1, 2, 3, 4, 5, 6 or 7, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

11. The method of claim 1, 2, 3, 4, 5, 6 or 7, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

12. The method of claim 1, 2, 3, 4, 5, 6 or 7, wherein the determining of the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data, and wherein the mathematical model is for determining the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data.

13. The method of claim 1, 2, 3, 4, 5, 6 or 7, wherein the level of RNA encoded by the gene

in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

14. The method of claim 13, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

15. The method of claim 1, 2, 4, 5, 6 or 7, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

16. The method of claim 15, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

17. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

18. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

inputting, to a computer, test data representing a level of RNA encoded by a CLEC4D gene in blood of the test subject; and

causing the computer to apply to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

19. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

inputting, to a computer, test data representing a level of RNA encoded by a IL2RB gene in blood of the test subject; and

causing the computer to apply to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

20. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

21. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

22. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

23. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer cancer, from test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject, the method comprising computer-implemented steps of:

(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and

(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

24. The method of claim 17, 18, 19, 20, 21, 22 or 23, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

25. The method of claim 17, 18, 19, 20, 21, 22 or 23, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

26. The method of claim 17, 18, 19, 20, 21, 22 or 23, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

27. The method of claim 26, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

28. The method of claim 17, 18, 20, 21, 22 or 23, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

29. The method of claim 28, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

30. A method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1:

(a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data;

(b) providing positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) determining a probability that the test data corresponds to the positive control data and not to the negative control data,

wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

31. The method of claim 30, wherein the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject.

32. The method of claim 30, further comprising determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA

encoded by the gene in blood of human control subjects not having colorectal cancer.

33. The method of claim 30, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

34. The method of claim 30, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

35. The method of claim 30, wherein the determining of the probability that the test data corresponds to the positive control data and not to the negative control data is effected by applying to the test data a mathematical model derived from the positive control data and from the negative control data, and wherein the mathematical model is for determining the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data.

36. The method of claim 30, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

37. The method of claim 36, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

38. The method of claim 30, wherein the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

39. The method of claim 38, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

40. A computer-based method of determining a probability that a human test subject has colorectal cancer as opposed to not having colorectal cancer, from test data representing a level of RNA encoded by the gene in blood of the test subject, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, computer-implemented steps of:
(a) applying to the test data a mathematical model derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data; and
(b) outputting the probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data,
wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

41. The method of claim 40, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

42. The method of claim 40, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

43. The method of claim 40, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

44. The method of claim 43, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

45. The method of claim 40, wherein the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

46. The method of claim 45, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

47. The method of claim 40, wherein the set of one or more genes consists of PRRG4.

48. The method of claim 40, wherein the set of one or more genes consists of IL2RB and PRRG4.

49. A kit comprising packaging and containing, for each gene of a set of two or more genes selected from the group consisting of ACTB, ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, a primer set capable of generating an amplification product of DNA complementary to RNA encoded, in a human subject, only by the gene.

50. The kit of claim 49, further containing two or more components selected from the group consisting of a thermostable polymerase, a reverse transcriptase, deoxynucleotide

triphosphates, nucleotide triphosphates and enzyme buffer.

51. The kit of claim 49, further containing at least one labeled probe capable of selectively hybridizing to either a sense or an antisense strand of the amplification product.

52. The kit of claim 49, further containing a computer-readable medium having instructions stored thereon that are operable when executed by a computer for applying a mathematical model to test data representing a level of RNA encoded by the gene in blood of a human test subject, wherein the mathematical model is derived from positive control data representing levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and from negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, wherein the mathematical model is for determining a probability that data representing a level of RNA encoded by the gene corresponds to the positive control data and not to the negative control data, and wherein the probability that the test data corresponds to the positive control data and not to the negative control data represents the probability that the test subject has colorectal cancer as opposed to not having colorectal cancer.

53. The kit of claim 49, wherein the set of one or more genes consists of ACTB and one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1.

54. The kit of claim 49, wherein the set of one or more genes consists of ACTB and ANXA3.

55. The kit of claim 49, wherein the set of one or more genes consists of ACTB and CLEC4D.

56. The kit of claim 49, wherein the set of one or more genes consists of ACTB and IL2RB.

57. The kit of claim 49, wherein the set of one or more genes consists of ACTB and LMNB1.

58. The kit of claim 49, wherein the set of one or more genes consists of ACTB and PRRG4.

59. The kit of claim 49, wherein the set of one or more genes consists of ACTB and TNFAIP6.

60. The kit of claim 49, wherein the set of one or more genes consists of ACTB and VNN1.

61. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1.

62. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and ANXA3.

63. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and CLEC4D.

64. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and LMNB1.

65. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and PRRG4.

66. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and TNFAIP6.

67. The kit of claim 49, wherein the set of one or more genes consists of IL2RB and VNN1.

68. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a ANXA3 gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

69. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a CLEC4D gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

70. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a IL2RB gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

71. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a LMNB1 gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

72. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:

(a) determining a level of RNA encoded by a PRRG4 gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human

control subjects not having colorectal cancer,
wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

73. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:
(a) determining a level of RNA encoded by a TNFAIP6 gene in blood of the test subject, thereby generating test data;
(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and
(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,
wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

74. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising:
(a) determining a level of RNA encoded by a VNN1 gene in blood of the test subject, thereby generating test data;
(b) providing negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and
(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,
wherein an indication by the value that the level of RNA encoded by the gene in blood of

the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

75. The method of claim 68, 69, 70, 71, 72, 73 or 74, wherein the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject.

76. The method of claim 68, 69, 70, 71, 72, 73 or 74, further comprising determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer.

77. The method of claim 68, 69, 70, 71, 72, 73 or 74, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

78. The method of claim 68, 69, 70, 71, 72, 73 or 74, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

79. The method of claim 68, 69, 70, 71, 72, 73 or 74, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

80. The method of claim 79, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

81. The method of claim 68, 69, 71, 72, 73 or 74, wherein the level of RNA encoded by the

gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

82. The method of claim 81, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

83. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:
(a) applying to test data representing a level of RNA encoded by a ANXA3 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and
(b) outputting the value,
wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

84. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:
(a) applying to test data representing a level of RNA encoded by a CLEC4D gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

85. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by a IL2RB gene gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

86. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by a LMNB1 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

87. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by a PRRG4 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

88. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by a TNFAIP6 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

89. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by a VNN1 gene in blood of the test subject and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer a mathematical formula for generating a value indicating whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(b) outputting the value,

wherein an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

90. The method of claim 83, 84, 85, 86, 87, 88 or 89, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

91. The method of claim 83, 84, 85, 86, 87, 88 or 89, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

92. The method of claim 83, 84, 85, 86, 87, 88 or 89, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

93. The method of claim 92, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction

analysis of RNA encoded by the gene and of RNA encoded by ACTB.

94. The method of claim 83, 84, 86, 87, 88 or 89, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

95. The method of claim 94, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

96. A method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1:

(a) determining a level of RNA encoded by the gene in blood of the test subject, thereby generating test data;

(b) providing negative control data representing levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer; and

(c) applying to the test data and to the negative control data a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer,

wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and wherein, for IL2RB, an indication by the value that the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

97. The method of claim 96, wherein the determining of the level of RNA encoded by the gene in blood of the test subject is effected by determining the level of RNA encoded by the gene in a blood sample isolated from the test subject.

98. The method of claim 96, further comprising determining levels of RNA encoded by the gene in blood of a population of human subjects having colorectal cancer, thereby providing the positive control data representing the levels of RNA encoded by the gene in blood of human control subjects having colorectal cancer, and determining levels of RNA encoded by the gene in blood of a population of human subjects not having colorectal cancer, thereby providing the negative control data representing the levels of RNA encoded by the gene in blood of human control subjects not having colorectal cancer.

99. The method of claim 96, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

100. The method of claim 96, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

101. The method of claim 96, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

102. The method of claim 101, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

103. The method of claim 96, wherein the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

104. The method of claim 103, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

105. A computer-based method of classifying a human test subject as more likely to have colorectal cancer than to not have colorectal cancer, the method comprising, for each gene of a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, computer-implemented steps of:

(a) applying to test data representing a level of RNA encoded by the gene in blood of the test subject, and to negative control data representing a level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, a formula for calculating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and indicating, for IL2RB, whether the level of RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer, and

(b) outputting the value,

wherein, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, an indication that the level of RNA encoded by the gene in blood of the test subject is higher than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer, and wherein, for IL2RB, an indication that the level of

RNA encoded by the gene in blood of the test subject is lower than the level of RNA encoded by the gene in blood of human control subjects not having colorectal cancer classifies the test subject as more likely to have colorectal cancer than to not have colorectal cancer.

106. The method of claim 105, wherein the level of RNA encoded by the gene in blood of the test subject is determined via quantitative reverse transcriptase-polymerase chain reaction analysis.

107. The method of claim 105, wherein the level of RNA encoded by the gene in blood of the test subject and the levels of RNA encoded by the gene in blood of the control subjects are determined via the same method.

108. The method of claim 105, wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by ACTB in blood of the test subject.

109. The method of claim 108, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by ACTB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by ACTB.

110. The method of claim 105, wherein the set of one or more genes is a set of one or more genes selected from the group consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, and wherein the level of RNA encoded by the gene in blood of the test subject is determined as a ratio to a level of RNA encoded by IL2RB in blood of the test subject.

111. The method of claim 110, wherein the level of RNA encoded by the gene in blood of the test subject and the level of RNA encoded by IL2RB in blood of the test subject are determined via duplex quantitative reverse transcriptase-polymerase chain reaction analysis of RNA encoded by the gene and of RNA encoded by IL2RB.

112. The method of claim 105, wherein the set of one or more genes consists of PRRG4.

113. The method of claim 105, wherein the set of one or more genes consists of IL2RB and PRRG4.

114. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a annexin A3 (ANXA3) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by ANXA3 as determined in step (i) with a level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

115. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a C-type lectin domain family 4, member D (CLEC4D) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

116. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a interleukin 2 receptor, beta (IL2RB) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood.

117. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a lamin B1 (LMNB1) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

118. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a proline rich Gla (G carboxyglutamic acid) 4 (transmembrane) (PRRG4) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

119. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a tumor necrosis factor, alpha induced protein

6 (TNFAIP6) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

120. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

(i) determining a level of RNA encoded by a vanin 1 (VNN1) gene in the test sample of blood,

(ii) comparing the level of RNA encoded by the gene as determined in step (i) with the level of the RNA encoded by the gene in control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood.

121. The method of claim 114, 115, 116, 117, 118, 119, or 120, wherein the control samples are from individuals who have been diagnosed as not having colorectal cancer.

122. A method of determining whether a test subject is at an increased risk of having colorectal cancer relative to the general population, comprising:

(a) obtaining a test sample of blood from the subject; and

for each gene of a set of genes selected from the group consisting of : ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1,

(i) determining a level of RNA encoded by the gene in the test sample of blood, thereby generating test data; and

(ii) applying to the the test data and to control data representing a level of RNA encoded by the gene in one or more control samples of blood a mathematical formula for generating a value indicating, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, whether the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and, for IL2RB, whether the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood; and

(b) concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, the value indicates that the level of RNA encoded by the gene in the test sample of blood is higher than in the control samples of blood, and concluding that the subject is at an increased risk of having colorectal cancer relative to the general population if, for IL2RB, the value indicates that the level of RNA encoded by the gene in the test sample of blood is lower than in the control samples of blood.

123. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

124. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a CLEC4D gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

125. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

126. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA,and an amplification product of the cDNA .

127. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a PRRG4 gene, cDN complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of th cDNA complementary to RNA, and an amplification product of the cDNA .

128. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

129. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

130. The composition of claim 123, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an

oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

131. The composition of claim 124, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDN complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

132. The composition of claim 125, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of th group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

133. The composition of claim 126, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of

the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

134. The composition of claim 127, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

135. The composition of claim 128, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and VNN1, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

136. The composition of claim 129, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and TNFAIP6, cDNA complementary to the RNA of the group of genes, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

137. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

138. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting o RNA encoded by an CLEC4D gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

139. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

140. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

141. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a PRRG4, gene, cDNA complementary to the

RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

142. An isolated composition comprising an isolated nucleic acid molecule of a blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

143. An isolated composition comprising a blood sample from a test subject and a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

144. The composition of claim 137, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of CLEC4D, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

145. The composition of claim 138, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, IL2RB, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the

complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

146. The composition of claim 139, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

147. The composition of claim 140, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, PRRG4, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

148. The composition of claim 141, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, TNFAIP6 and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes

under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

149. The composition of claim 142, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and VNN1, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

150. The composition of claim 143, further comprising a nucleic acid molecule selected from one or more of the group consisting of RNA encoded by one or more genes selected from the group of genes consisting of ANXA3, CLEC4D, IL2RB, LMNB1, PRRG4, and TNFAIP6, cDNA complementary to the RNA of the group of genes or the complement thereof, an oligonucleotide which specifically hybridizes to the cDNA complementary to the RNA of the group of genes or to the RNA of the group of genes under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA of the group of genes, and an amplification product of the cDNA of the RNA of the group of genes.

151. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof.

152. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of

encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

153. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

154. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

155. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof.

156. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, or composition thereof.

157. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an ANXA3 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA

complementary to RNA of encoded by a CLEC4D gene, or composition thereof.

158. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof.

159. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

160. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

161. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

162. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof.

163. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an CLEC4D gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, or composition thereof.

164. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

165. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

166. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, or composition thereof.

167. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an IL2RB gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof.

168. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of

encoded by a LMNB1 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, or composition thereof.

169. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a LMNB1 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

170. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by an LMNB1 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof.

171. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, or composition thereof.

172. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a PRRG4 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

173. A primer set comprising a first primer, wherein the first primer is one of a set of primers capable of generating an amplification product of cDNA complementary to RNA of encoded by a VNN1 gene, and a second primer, wherein the second primer primer is one of a set of primers capable of generating an amplification product of cDNA

complementary to RNA of encoded by a TNFAIP6 gene, or composition thereof.

174. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an ANXA3 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

175. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a CLEC4D, gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

176. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an IL2RB gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA .

177. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by an LMNB1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

178. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a PRRG4 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

179. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a TNFAIP6 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

180. A test system comprising:

a) two or more blood samples wherein each blood sample is from a different test subject, and

b) an isolated nucleic acid molecule of each the blood sample from a test subject, wherein the nucleic acid molecule is selected from one or more of the group consisting of RNA encoded by a VNN1 gene, cDNA complementary to the RNA, an oligonucleotide which specifically hybridizes to the cDNA or complement thereof, or the RNA under stringent conditions, a primer set capable of generating an amplification product of the cDNA complementary to RNA, and an amplification product of the cDNA.

181. The test system of any one of claims 173 through 180, wherein the test subject is being screened for colorectal cancer.

SEQUENCE LISTING

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<120> METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT

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ACTB: actin, beta SEQ ID NO:73

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FIG. 1A

ANXA3: annexin A3 SEQ ID NO:74

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1621 aaaaaaaaaa aaaa

FIG. 1B

CLEC4D: C-type lectin domain family 4, member D (SEQ ID NO:75)

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1921 gtggtctttc ttaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa
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FIG. 1C

IL2RB: interleukin 2 receptor, beta (SEQ ID NO:76)

```
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2821 cctgggacct cccactgccc cctccactgg aggggtctcc tctgcagctc agggactggc
2881 acactggcct ccagaagggc agctccacag ggcagggcct cattattttt cactgcccca
2941 gacacagtgc ccaacacccc gtcgtatacc ctggatgaac gaattaatta cctggcacca
```

FIG. 1D (part 1/2)

3001 cctcgtctgg gctccctgcg cctgacattc acacagagag gcagagtccc gtgcccatta
3061 ggtctggcat gccccctcct gcaaggggct caaccccta ccccgacccc tccacgtatc
3121 tttcctaggc agatcacgtt gcaatggctc aaacaacatt ccaccccagc aggacagtga
3181 ccccagtccc agctaactct gacctgggag ccctcaggca cctgcactta caggccttgc
3241 tcacagctga ttgggcacct gaccacacgc ccccacaggc tctgaccagc agcctatgag
3301 ggggtttggc accaagctct gtccaatcag gtaggctggg cctgaactag ccaatcagat
3361 caactctgtc ttgggcgttt gaactcaggg agggaggccc ttgggagcag gtgcttgtgg
3421 acaaggctcc acaagcgttg agccttggaa aggtagacaa gcgttgagcc actaagcaga
3481 ggaccttggg ttcccaatac aaaaatacct actgctgaga gggctgctga ccatttggtc
3541 aggattcctg ttgcctttat atccaaaata aactcccctt tcttgaggtt gtctgagtct
3601 tgggtctatg ccttgaaaaa agctgaatta ttggacagtc tcacctcctg ccatagggtc
3661 ctgaatgttt cagaccacaa ggggctccac acctttgctg tgtgttctgg ggcaacctac
3721 taatcctctc tgcaagtcgg tctccttatc cccccaaatg gaaattgtat ttgccttctc
3781 cactttggga ggctcccact tcttgggagg gttacatttt ttaagtctta atcatttgtg
3841 acatatgtat ctatacatcc gtatctttta atgatccgtg tgtaccatct ttgtgattat
3901 ttccttaata tttttctttt aagtcagttc attttcgttg aaatacattt atttaaagaa
3961 aaatctttgt tactctgtaa atgaaaaaac ccattttcgc tataaataaa aggtaactgt
4021 acaaaataag tacaatgcaa caaaa

FIG. 1D (part 2/2)

LMNB1: lamin B1 (SEQ ID NO:77)

```
   1 gtgcagcctg agaggaaaca aagtgctgcg agcaggagac ggcggcggcg cgaaccctgc
  61 tgggcctcca gtcaccctcg tcttgcattt tcccgcgtgc gtgtgtgagt gggtgtgtgt
 121 gttttcttac aaagggtatt tcgcgatcga tcgattgatt cgtagttccc ccccgcgcgc
 181 ctttgccctt tgtgctgtaa tcgagctccc gccatcccag gtgcttctcc gttcctctaa
 241 acgccagcgt ctggacgtga gcgcaggtcg ccggtttgtg ccttcggtcc ccgcttcgcc
 301 ccctgccgtc ccctccttat cacggtcccg ctcgcggcct cgccgccccg ctgtctccgc
 361 cgcccgccat ggcgactgcg acccccgtgc cgccgcggat gggcagccgc gctggcggcc
 421 ccaccacgcc gctgagcccc acgcgcctgt cgcggctcca ggagaaggag gagctgcgcg
 481 agctcaatga ccggctggcg gtgtacatcg acaaggtgcg cagcctggag acggagaaca
 541 gcgcgctgca gctgcaggtg acggagcgcg aggaggtgcg cggccgtgag ctcaccggcc
 601 tcaaggcgct ctacgagacc gagctggccg acgcgcgacg cgcgctcgac gacacggccc
 661 gcgagcgcgc caagctgcag atcgagctgg gcaagtgcaa ggcggaacac gaccagctgc
 721 tcctcaacta tgctaagaag gaatctgatc ttaatggcgc ccagatcaag cttcgagaat
 781 atgaagcagc actgaattcg aaagatgcag ctcttgctac tgcacttggt gacaaaaaaa
 841 gtttagaggg agatttggag gatctgaagg atcagattgc ccagttggaa gcctccttag
 901 ctgcagccaa aaaacagtta gcagatgaaa ctttacttaa agtagatttg gagaatcgtt
 961 gtcagagcct tactgaggac ttggagtttc gcaaaagcat gtatgaagag gagattaacg
1021 agaccagaag gaagcatgaa acgcgcttgg tagaggtgga ttctgggcgt caaattgagt
1081 atgagtacaa gctggcgcaa gcccttcatg agatgagaga gcaacatgat gcccaagtga
1141 ggctgtataa ggaggagctg gagcagactt accatgccaa acttgagaat gccagactgt
1201 catcagagat gaatacttct actgtcaaca gtgccaggga agaactgatg gaaagccgca
1261 tgagaattga gagcctttca tcccagcttt ctaatctaca gaaagagtct agagcatgtt
1321 tggaaaggat tcaagaatta gaggacttgc ttgctaaaga aaaagacaac tctcgtcgca
1381 tgctgacaga caaagagaga gagatggcgg aaataaggga tcaaatgcag caacagctga
1441 atgactatga acagcttctt gatgtaaagt tagccctgga catggaaatc agtgcttaca
1501 ggaaactctt agaaggcgaa gaagagaggt tgaagctgtc tccaagccct tcttcccgtg
1561 tgacagtatc ccgagcatcc tcaagtcgta gtgtacgtac aactagagga aagcggaaga
1621 gggttgatgt ggaagaatca gaggcgagta gtagtgttag catctctcat tccgcctcag
1681 ccactggaaa tgtttgcatc gaagaaattg atgttgatgg gaaatttatc cgcttgaaga
1741 acacttctga acaggatcaa ccaatgggag gctgggagat gatcagaaaa attggagaca
1801 catcagtcag ttataaatat acctcaagat atgtgctgaa ggcaggccag actgttacaa
1861 tttgggctgc aaacgctggt gtcacagcca gccccccaac tgacctcatc tggaagaacc
1921 agaactcgtg gggcactggc gaagatgtga aggttatatt gaaaaattct cagggagagg
1981 aggttgctca aagaagtaca gtctttaaaa caaccatacc tgaagaagag gaggaggagg
2041 aagaagcagc tggagtggtt gttgaggaag aacttttcca ccagcaggga accccaagag
2101 catccaatag aagctgtgca attatgtaaa attttcaact gtcttcctca aaataaagaa
2161 gtatggtaat ccttacctgt atacagtgca gagccttctc agaagcacag aatattttta
2221 tatttccttt atgtgaattt ttaagctgca aatctgatgg ccttaatttc ctttttgaca
2281 ctgaaagttt tgtaaaagaa atcatgtcca tacactttgt tgcaagatgt gaattattga
2341 cactgaactt aataactgtg tactgttcgg aaggggttcc tcaaattttt tgactttttt
2401 tgtatgtgtg tttttttcttt tttttaagt tcttatgagg aggggagggt aaataaacca
2461 ctgtgcgtct tggtgtaatt tgaagattgc ccatctaga ctagcaatct cttcattatt
2521 ctctgctata tataaaacgg tgctgtgagg gaggggaaaa gcatttttca atatattgaa
2581 cttttgtact gaattttttt gtaataagca atcaaggtta taattttttt taaaatagaa
2641 attttgtaag aaggcaatat taacctaatc accatgtaag cactctggat gatggattcc
2701 acaaaacttg gttttatggt tacttcttct cttagattct taattcatga ggagggtggg
2761 ggagggaggt ggagggaggg aagggtttct ctattaaaat gcattcgttg tgttttttaa
2821 gatagtgtaa cttgcttaaa tttcttatgt gacattaaca aataaaaaag ctcttttaat
2881 at
```

FIG. 1E

PRRG4: proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane) (SEQ ID NO:78)

```
   1 cccggaccga ggcaggacct caccccgcgc gtgttccccg ggcgcccctc tgcgaacccc
  61 aggcccttcc caggtttgcg cgcgggggcc atccagaccc tgcggagagc gaggcccgga
 121 gcgtcgccga ggtttgaggg cgcccggagac cgagggcctg gcggccgaag gaaccgcccc
 181 aagaagagcc tctggcccgg gggctgctgg aacatgtgcg gggggacaca gtttgtttga
 241 cagttgccag actatgttta cgcttctggt tctactcagc caactgccca cagttaccct
 301 ggggtttcct cattgcgcaa gaggtccaaa ggcttctaag catgcgggag aagaagtgtt
 361 tacatcaaaa gaagaagcaa actttttcat acatagacgc cttctgtata atagatttga
 421 tctggagctc ttcactcccg gcaacctaga aagagagtgc aatgaagaac tttgcaatta
 481 tgaggaagcc agagagattt ttgtggatga agataaaacg attgcatttt ggcaggaata
 541 ttcagctaaa ggaccaacca caaaatcaga tggcaacaga gagaaaatag atgttatggg
 601 ccttctgact ggattaattg ctgctggagt atttttggtt atttttggat tacttggcta
 661 ctatctttgt atcactaagt gtaataggct acaacatcca tgctcttcag ccgtctatga
 721 aagggggagg cacactccct ccatcatttt cagaagacct gaggaggctg ccttgtctcc
 781 attgccgcct tctgtggagg atgcaggatt accttcttat gaacaggcag tggcgctgac
 841 cagaaaacac agtgtttcac caccaccacc atatcctggg cacacaaaag gatttagggt
 901 atttaaaaaa tctatgtctc tcccatctca ctgactacct tgtcattttg gtataagaaa
 961 tttgtgttat ttgataggcc gggcatggtg gctcatgcct gtaatcccag cactttggga
1021 ggccaggagt tcgagaccag cctggccaac atggtgaaac ccggtctcta ctaaaaattc
1081 aaaaattacc taggcgtcat ggggcatgcc tgtagtccca cctacttggg aggctgaagc
1141 aggagaattg ctcgaacctg ggaggcagag gttgcagtaa gctgagatca cgccactgca
1201 ttccagcctg ggcgacagag caagactcca tctcaaaaat aaaataaaaa aagaaagaaa
1261 gaaaagaaga agaaaagaga agaaggagaa ggagatgaag gaggaggagg aggagaagga
1321 gaagaagaag aagaagaaga ccacaaaaga catgactatc caacttttta tgacaaactg
1381 caaggaataa aggaagaata agtccatgta ctgtaccaca gaagttctgt ctgcatcttg
1441 gacctgaact tgatcattat cagcttgata agagactttt tgactctata tccttgcagt
1501 taagaagaaa gcactttttt gtaatgtttg ttttaatggt tcaaaaaaaa tctttcttat
1561 aaagagcata ggtagaatta gtgaactctt tggatccttt gtacagataa aggttataga
1621 tttcttgtgt tgaatattaa aaaagcaagg atgtctaacc attaagatta tccaaagtca
1681 ggctggcgc agtggctcac gcctgtaatc ccagcacttt gggagggata ggtgggcgga
1741 tcacctgagg tcaggagttt gagaccagcc tggccaacat ggcaaaaccc cgtctctaca
1801 aaaatacaaa agaaattagc cagacatgat ggcgggtgcc tctaatccca gctactgggg
1861 aggctgaggt gggagaatcg cttgaactcg ggaggtggag gttgtagtga ggcgagattg
1921 tgccattgca ctccaacctg ggcgacagag tgagactcca tctcaaaaaa aaaaaaaaaa
1981 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa
```

FIG. 1F

TNFAIP6: tumor necrosis factor, alpha-induced protein 6 (SEQ ID NO:79)

```
   1 cagtcacatt tcagccactg ctctgagaat ttgtgagcag cccctaacag gctgttactt
  61 cactacaact gacgatatga tcatcttaat ttacttattt ctcttgctat gggaagacac
 121 tcaaggatgg ggattcaagg atggaatttt tcataactcc atatggcttg aacgagcagc
 181 cggtgtgtac cacagagaag cacggtctgg caaatacaag ctcacctacg cagaagctaa
 241 ggcggtgtgt gaatttgaag gcggccatct cgcaacttac aagcagctag aggcagccag
 301 aaaaattgga tttcatgtct gtgctgctgg atggatggct aagggcagag ttggataccc
 361 cattgtgaag ccagggccca actgtggatt tggaaaaact ggcattattg attatggaat
 421 ccgtctcaat aggagtgaaa gatgggatgc ctattgctac aacccacacg caaaggagtg
 481 tggtggcgtc tttacagatc caaagcaaat ttttaaatct ccaggcttcc caaatgagta
 541 cgaagataac caaatctgct actggcacat tagactcaag tatggtcagc gtattcacct
 601 gagttttttta gattttgacc ttgaagatga cccaggttgc ttggctgatt atgttgaaat
 661 atatgacagt tacgatgatg tccatggctt tgtgggaaga tactgtggag atgagcttcc
 721 agatgacatc atcagtacag gaaatgtcat gaccttgaag tttctaagtg atgcttcagt
 781 gacagctgga ggtttccaaa tcaaatatgt tgcaatggat cctgtatcca aatccagtca
 841 aggaaaaaat acaagtacta cttctactgg aaataaaaac tttttagctg gaagatttag
 901 ccacttataa aaaaaaaaaa aaggatgatc aaaacacaca gtgtttatgt tggaatcttt
 961 tggaactcct ttgatctcac tgttattatt aacatttatt tattattttt ctaaatgtga
1021 aagcaataca taatttaggg aaaattggaa aatataggaa actttaaacg agaaaatgaa
1081 acctctcata atcccactgc atagaaataa caagcgttaa cattttcata tttttttctt
1141 tcagtcattt ttctatttgt ggtatatgta tatatgtacc tatatgtatt tgcatttgaa
1201 attttggaat cctgctctat gtacagtttt gtattatact ttttaaatct tgaactttat
1261 aaacattttc tgaaatcatt gattattcta caaaaacatg attttaaaca gctgtaaaat
1321 attctatgat atgaatgttt tatgcattat ttaagcctgt ctctattgtt ggaatttcag
1381 gtcattttca taaatattgt tgcaataaat atccttgaac acaaaaaaaa aaaaaaaaaa
```

FIG. 1G

VNN1: vanin 1 (SEQ ID NO: 80)

```
   1 cattggactt cagcatgact actcagttgc cagcttacgt ggcaatttg ctttctatg
  61 tctcaagagc cagctgccag gacactttca ttgcagctgt ttatgagcat gcagcgatat
 121 tgcccaatgc caccctaaca ccagtgtctc gtgaggaggc tttggcatta atgaatcgga
 181 atctggacat tttggaagga gcgatcacat cagcagcaga tcagggtgcg catattattg
 241 tgactccaga agatgctatt tatggctgga acttcaacag ggactctctc tacccatatt
 301 tggaggacat cccagaccct gaagtaaact ggatcccctg taataatcgt aacagatttg
 361 gccagacccc agtacaagaa agactcagct gcctggccaa gaacaactct atctatgttg
 421 tggcaaatat tggggacaag aagccatgcg ataccagtga tcctcagtgt cccccctgatg
 481 gccgttacca atacaacact gatgtggtat ttgattctca aggaaaactg gtggcacgct
 541 accataagca aaaccttttc atgggtgaaa atcaattcaa tgtacccaag gagcctgaga
 601 ttgtgacttt caataccacc tttggaagtt ttggcatttt cacatgcttt gatatactct
 661 tccatgatcc tgctgttacc ttggtgaaag atttccacgt ggacaccata gtattcccaa
 721 cagcttggat gaatgttttg ccacatttgt cagctgttga attccactca gcttgggcta
 781 tgggcatgag ggtcaatttc cttgcatcca acatacatta cccctcaaag aaaatgacag
 841 gaagtggcat ctatgcaccc aattcttcaa gagcatttca ttatgatatg aagacagaag
 901 agggaaaact cctcctctcg caactggatt cccacccatc ccattctgca gtggtgaact
 961 ggacttccta tgccagcagt atagaagcgc tctcatcagg aaacaaggaa tttaaaggca
1021 ctgtcttttt cgatgaattc acttttgtga agctcacagg agttgcagga aattatacag
1081 tttgtcagaa agatctctgc tgtcatttaa gctacaaaat gtctgagaac ataccaaatg
1141 aagtgtacgc tctaggggca tttgacggac tgcacactgt ggaagggcgc tattatctac
1201 agatttgtac cctgttgaaa tgtaaaacga ctaatttaaa cacttgcggt gactcagctg
1261 aaacagcttc taccaggttt gaaatgttct ccctcagtgg cactttcgga acccagtatg
1321 tctttcctga ggtgttgctg agtgaaaatc agcttgcacc tggagaattt caggtgtcaa
1381 ctgacggacg cttgtttagt ctgaagccaa catccggacc tgtcttaaca gtaactctgt
1441 ttgggaggtt gtatgagaag gactgggcat caaatgcttc atcaggcctc acagcacaag
1501 caagaataat aatgctaata gttatagcac ctattgtatg ctcattaagt tggtagaata
1561 ttgacttttt ctctttttta tttgggataa tttaaaaaat gatggatgag aaaagaaaga
1621 ttggtccggg ttaatattat cctctagtat aagtgaatta ctagtttctc tttatttaga
1681 caaacacaca cacaccagat aatataaact taataaatta tctgttaatg tagattttat
1741 ttaaaaaact atatttgaac attggtcttt cttggacgtg agctaattat atcaaataag
1801 tatcacaaat cttttacgca gaagaaataa aaactacggg tagaaaacat aagaactatc
1861 ataaaattta cttacaagga ggctgctctt gttaccactt ttattatatt acgtatcact
1921 tattcagctc tgctgaaaat ttccaatgac tttgtttgtt tgctctttta gtttttttacc
1981 taaacaatac attttgattc tcttgtgggt tgataatgtc tccccaaaat ttacatgttg
2041 aagcacctca gaatgtgact gtatttggag acagggtctt taaagaggta aaataaggtc
2101 attaggatag accctaattc aatatgactg atgatcataa aagaagaggc gagtagggca
2161 caacaggcac aaagggagac cataaggaga cacagaggaa ggacaactct ttacaagcta
2221 agaagagagg gcctcagaag aaaccaaccc tgccaacacc ttgatcttgg acttccagcc
2281 tccaaaacta tgagaaataa atttctattg tttaagtcac ccagtccatg gtactttgtt
2341 aggcagccct ggcaaatgaa tcaaagaccc attcctgttc ctctccccac cactactgtt
2401 ttctactgta atctgaagct tcaacaaaag gcttacctgg taagaatatt cagctggtct
2461 gggtcctcaa gactccaata gacactctta aagaaggatt gctgatggat tgatagtgaa
2521 accattagat cattgaattc ctctggaatt agaaaaccag agagtcccat tttaagaaat
2581 tagatattta atatagcatt gtgtgttcta ttttagtaac agcagaatct cttgacatta
2641 cacaactcag tgaaacaaca tcatttaagc caaaatatct cccaactgac tgatagactc
2701 tgagcactaa tatcatagtg ctgtgatgat ggacaattac atagtaccga taacagccat
2761 gcactgtgca aagcatgccc ttctgcacag gagagcaagg cacttgcagt agtgatctat
2821 gccagcaaaa catcatttg agacaaacat ttttgtggca gatgtttttc ctaaaaagta
2881 ctatatcatc caagaaatat ttgagtaaaa tcccttgttc ttttgggtga cattaactga
2941 catttgcttt ttttcaagac ctaatagaaa ataagaaagc ccataatgta tttagaaaca
3001 ggaatcctca gagcaattct ctgtattctc atataatttc aatgtaaaac agaaaacata
3061 ttgatgtgtt ggtgataggc ttgaattatt aaaaacttca aaaacaaaa
```

FIG. 1H

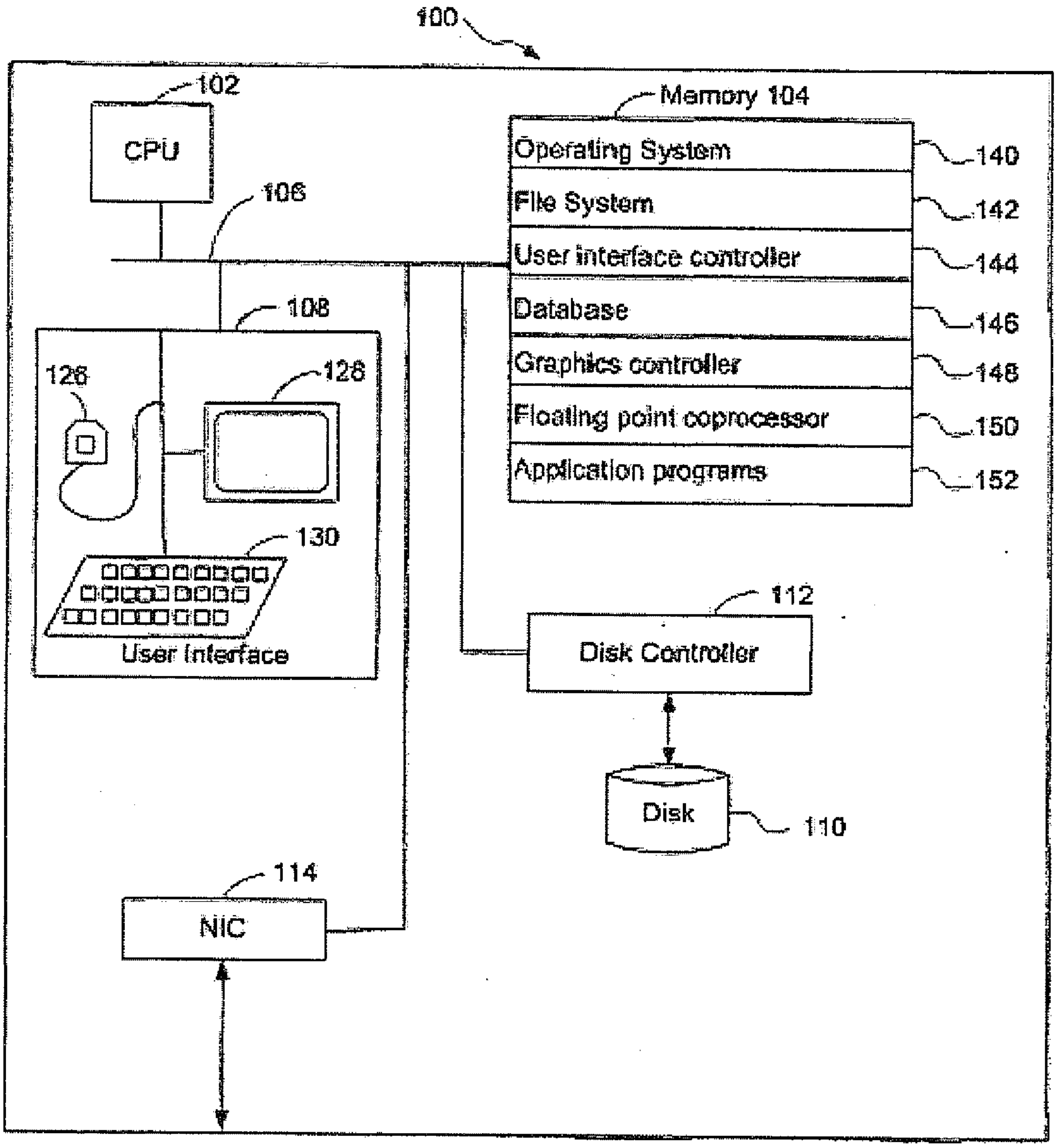
100
102
CPU
Memory 104
Operating System
140
File System
142
106
User interface controller
144
Database
146
108
126
128
Graphics controller
148
Floating point coprocessor
150
Application programs
152
130
112
User Interface
Disk Controller
Disk
110
114
NIC

FIG. 2