Epigenetic Biomarkers for Noninvasive Detection of Colorectal Cancer

Dhruvajyoti Roy1, David Taggart4, Lianghong Zheng2, Dan Liu2, Gen Li2, Mingzhen Li2, Kang Zhang1,3, and Richard A. Van Etten1,5
1Laboratory for Advanced Medicine, Inc., Irvine, CA, USA; 2Laboratory for Advanced Medicine, Inc., Beijing, China; 3Institute for Genomic Medicine, University of California at San Diego, La Jolla, CA, USA; 4Laboratory for Advanced Medicine, Inc., West Lafayette, IN, USA; 5Chao Family Comprehensive Cancer Center, University of California at Irvine, Irvine, CA, USA

Abstract

Background: Aberrant DNA methylation is known to be a major mechanism for inactivation of cancer-associated genes. Including tumor suppressor genes, is a colorectal cancer (CRC) and in other human cancers. Cancer-specific DNA methylation patterns of peripheral DNA (cfDNA) isolated from total samples is a non-invasive method to determine representative epigenetic aberrations often missed in solid tumors. In this study, we identified and validated colorectal cancer-specific methylation markers from cfDNA. We also compared the relative amount of cfDNA methylation in CRC patients to healthy controls and compared the characteristics of these markers. We calculated the relative amount of cfDNA methylation in CRC patients to healthy controls and compared the characteristics of these markers. We calculated the relative amount of cfDNA methylation in CRC patients to healthy controls and compared the characteristics of these markers.

Methods: For marker validation, a total of 154 samples drawn from 84 subjects diagnosed with colorectal cancer (Stage I to IV), 24 healthy donors, 14 subjects with benign colorectal diseases, and 20 subjects diagnosed with other cancer types (breast, lung and liver 10 cases each) were obtained for a randomized, blinded study. Cell-free DNA was then extracted from the samples, bisulfite converted, and DNA methylation was quantified using the Illumina Platform.

Results: For quantifying DNA methylation at the target sites, colorectal cancer samples were differentiated from samples drawn from healthy subjects or subjects with benign disease with an overall sensitivity of 95% and specificity of 80%. A total of 10 to 15 markers were selected for the study with 100% sensitivity and 91% specificity as a colorectal cancer marker for the assay, for a calculated specificity of 100%.

Conclusions: These results demonstrate the high diagnostic potential of DNA methylation markers isolated from blood for the detection of colorectal cancer. Together, these findings establish the utility of methylation biomarkers for the detection of colorectal cancer even as early as Stage I. In addition, a quantitative analysis of cfDNA provides an opportunity for non-invasive detection and monitoring of disease.

Introduction

Colorectal Cancer Infographics

Blood-based liquid biopsy for cancer detection: major analytes

Oncogenesis Alters DNA Methylation Patterns

Marker Selection, Screening and Validation

Marker Selection in Silico

Marker Screening Targeted Bisulfite Sequencing

Marker Validation IVyGene Platform

Oncogenicity Alters DNA Methylation Patterns

Results

Validation Study Cohort

Colorectal Cancer

Normal

Benign Disease

Other Cancers

Breast Cancer

Liver Cancer

Lung Cancer

Total

<ref>

Sensitivity

Specificity

Comparisons to Current Techniques

IvyGene On Colorectal Cancer test

CF-DNA and FIT have reported sensitivities of 50% and 75% respectively, and specificities of 77% and 89%.

Conclusions

The IvyGene On Colorectal Cancer test has been developed to detect colorectal cancer at an early stage with a high degree of sensitivity and specificity.

Benign disease can be differentiated from colorectal cancer by quantifying methylation of cfDNA.

Patient outcomes are predicted to improve by detecting colorectal cancer at an early stage.

References:


www.lamoncogroup.com
https://www.ivygenelabs.com
Email: info@ivygenelabs.com
Phone: 844-489-4363