A Fresh Method Using Multi-Omics and Whole-Part Relationships to Look for Factors that Influence the Course of Colorectal Cancer

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Abstract

It is especially crucial to develop ways to acquire molecules with meaningful diagnostic effects due to the high prevalence and mortality of Colorectal Cancer (CRC) and the absence of effective diagnostic molecules, which have resulted in poor treatment outcomes for colorectal cancer. To uncover individual and co-pathways of change in early-stage and colorectal malignancies and to learn the factors that contribute to the development of colorectal cancer, we proposed a whole and part study strategy (early-stage colorectal cancer as "part" and colorectal cancer as "whole"). The pathological state of tumour tissue may not always be reflected by metabolite indicators found in plasma. Multi-omics analyses of 128 plasma metabolomes and 84 tissue transcriptomes were conducted on three phases of biomarker discovery research (discovery, identification, and validation) in order to investigate the determining biomarkers linked to plasma and tumour tissue in the course of CRC. Importantly, we note that patients with colorectal cancer had much greater metabolic levels of oleic acid and FA than did healthy individuals. Oleic acid and FA (18:2) can both stimulate the growth of colorectal cancer tumour cells and serve as plasma biomarkers for the early stages of the disease, according to biofunctional verification. Our work offers a promising tool for the clinical detection of colorectal cancer, and we suggest a unique research approach to identify co-pathways and significant biomarkers that may be targeted for a possible role in early colorectal cancer.

Keywords: Transcriptomes; Colorectal cancer; Plasma biomarkers; Diagnostic molecules

Introduction

Colorectal cancer (CRC), a cancer with a high incidence and mortality rate, continues to be the second-leading cause of cancer-related deaths worldwide. Alterations in metabolic indicators have been associated with disease stages and survival rates in CRC. Usually, clinical signs generally appear in the progressed stage of colorectal cancer, far behind the time that abnormal metabolite changes appear in the blood. The concealment of CRC diagnosis warrants attention and makes active population screening which has been well-proven to save lives become a diagnostic necessity. Colonoscopy is the gold standard for the early visual detection and screening of CRC. However, it is an expensive, intrusive procedure that requires uncomfortable intestinal preparation and could result in problems. The need for non-invasive biomarkers that are specific and sensitive for the early diagnosis of CRC is suggested by the possibility that these invasive diagnostic techniques will have a negative impact on patient compliance with advised screening. However, because to their low sensitivity—for instance, the serum carcinoembryonic antigen (CEA) detection sensitivity is about 40–60%—the development of useful non-invasive diagnostic approaches has been constrained in clinical diagnosis. Although it has good specificity but average sensitivity, the faecal occult blood test (FOBT), a well-known non-invasive test for the identification of CRC precursors, is particularly suitable for patients having blood in the faeces. Therefore, novel non-invasive screening methods and biomarkers are required to detect CRC and its precursors in easily accessible biospecimens. In the interdisciplinary science of metabolomics, which complements genomes, transcriptomics, and proteomics, metabolites are directly tied to phenotypes and reflect ongoing activities in cells or organisms. Metabolites, which are closely related to phenotypes, represent how a cell or organism is functioning. Several detection technologies, most notably mass spectrometry, are employed to retrieve specific information from complex multidimensional data. Particularly in the case of illnesses with asymptomatic progression, the metabolic properties of the human body at various physiological and pathological stages might be employed as diagnostic or prognostic biomarkers to identify disease progression. As a result, using metabolomics approaches to look at related markers can be very helpful in diagnosing colorectal cancer. In plasma and serum, a number of possible CRC markers have been identified.Metabolomics, however, can only discover biomarkers. The pathophysiology of CRC is not seen differently by each new biomarker. Transcriptomics has been found to assist understand the mechanisms behind diseases and allows us to observe pathological changes at the genomic level. Transcriptomics is therefore useful for identifying targets for either diagnostic or therapeutic purposes. Recent research has shown important developments in the molecular pathways underlying colorectal cancer's transcriptomics. However, transcription is not a continuous process because it happens in small bursts and varies from gene to gene.Integrating multi-omics data can reveal important roles in both health and disease. Additionally, multi-omics profiling is widely used in early diagnostic analysis of colorectal cancer due to the shortcomings and complementarity of metabolomics and transcriptomics. Combining metabolomics and transcriptomics could result in a deeper comprehension of the pathophysiology of CRCs than either technique working independently. The validity of possible diagnostic biomarkers would be improved by examining both facets because both metabolite dysregulation and dysregulation of gene expression occur during the same biological event. However, when the results are simply examined in conjunction with multi-omics, it is equally challenging to evaluate the outcome as a determinant of colorectal cancer progression. Previous studies have examined each stage of colorectal cancer separately, but doing so does not provide for a comprehensive understanding of how the disease progresses, making it challenging to identify the crucial points. In order to reach the best outcome, it is necessary for us to develop a holistic perspective that is focused on the "whole" and to keep our attention on the complete problem. Early CRC and advanced CRC were considered to be "part" of the colorectal cancer growth process, with the "whole" playing a dominant role, setting the direction for the "part," and possessing a destructive force that each stage of cancer does not possess. Changes to important components even have a promotion effect on the entire cancer process. The determinant in the CRC procession is difficult to find since the dialectical relationship between the "part" and the "whole" has been overlooked. To increase the accuracy of CRC early diagnosis, the "part" and the "whole" should be treated dialectically, and their relationship should be urged. Here, we provide a novel approach to analyse both the "whole" and the "part", and their co-pathways were researched and the alterations were assessed by the suggested combining method of metabolomics and transcriptomics. In this study, the unique changing metabolic pathways and co-changing metabolic pathways of early and advanced colorectal cancer were compared to find and validate novel biomarkers and test their clinical utility. A total of 128 plasma metabolomes and 84 tissue transcriptomes of patients with CRC were analysed to explore abnormal metabolic pathways associated with colorectal cancer.

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