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INTEGRATIVE ANALYSIS OF FECAL METAGENOMICS AND METABOLOMICS IN COLORECTAL CANCER

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Resumen

Introduction: Colorectal cancer (CRC) is the second leading cause of death in developed countries and the most common cancer in Spain. Despite the availability of a gold standard diagnostics biomarker such as Fecal Occult Blood Test (FOB), their accuracy for the early stages of the disease is suboptimal. In this study, we performed a combination of metabolomics and microbiome analyses in feces samples in order to identify and characterize potential early biomarkers for both advanced adenomas (AD) and CRC.

Methods: We performed UHPLC-MS and V1-V2 16S rDNA sequencing on 245 fecal samples: 77 controls (C), 69 AD and 99 CRC patients. Results obtained through each omics approach were studied per separate and later combined them by a range of methodologies in order to identify potential interactions between the microbiome and fecal metabolome. We finally generated a combined metabolomics-microbiome model for CRC diagnosis.

Results: We report differences in fecal levels of cholesteryl esters, sphingomyelins and ceramides in CRC patients when compared to C and AD samples. We also identified a trend of AD patients to have elevated triacylglycerols and diacylglycerols when compared to C samples. We identified 3 genera to be increased in CRC patients (*Fusobacterium, Parvimonas* and *Staphylococcus)* and *Lachnospiraceae* family to be reduced in these patients. We finally described *Adlercreutzia* to be more abundant in AD patients' feces when compared to both control and CRC samples, suggesting a potential utility as biomarker for early stages of CRC disease. Microbiome composition identified alterations were associated to proinflammatory events and to a metabolism shift towards carbohydrates degradation and fermentation, leading to a reduction of short-chain fatty acids, including also several methane-related metabolic pathways, supporting the presence of anaerobic bacteria in this population. Then, we combined both datasets and identified a number of correlations between altered metabolites and altered genera in CRC patients.

Conclusions: We describe a relevant similarity between both datasets, thus confirming the important role of gut microbiota on fecal metabolome. Finally, using the combination of metabolomics and microbiome data, we propose a diagnostics logistic model that outperforms single-omics ones and FOB discriminative capabilities.

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