Untargeted serum metabolite profiling of colorectal cancer using GC-Orbitrap technology

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Globally affecting more than one million new persons each year, and killing more than 700,000, colorectal cancer is the second leading cause of cancer-related deaths in women and the third in men. Nevertheless, diagnosis is still largely based on invasive tissue sampling, while gaps remain in the understanding of its pathogenesis, with complex combinations between lifestyle, genetics, epigenetics, chronic inflammation (IBD) and microbiota. Untargeted metabolomics is one way to address these issues. Through metabolite profiling, it provides a picture of the outcome of the disease. To do so, significant variations between pathological and healthy phenotypes have to be found, and the responsible metabolites must be confidently identified. In this study, the ability of the Q Exactive GC-MS Orbitrap system to detect and identify metabolites related to colorectal cancer in an untargeted manner was assessed. The workflow uses the advantages of high peak capacity and chromatographic resolution of gas chromatography with the high resolution and sub-ppm mass accuracy of the Orbitrap mass spectrometer. The samples analyzed belonged to two populations linked to colorectal adenocarcinoma (active and remission, 12 samples each) along with two controls cohorts of the same size specifically matched for possible biases (gender, age, BMI, smoking status etc.), and pooled QC samples. Analytical raw data files were automatically processed through two software platforms specifically designed for the Orbitrap technology (TraceFinder™ and Compound Discoverer™). Compound identification was made using existing commercial libraries as well as an in-house developed high resolution Orbitrap metabolomics library.