

DISCRIMINATION BETWEEN INFLAMMATORY BOWEL DISEASE (IBD) PHENOTYPES BY GC×GC-HRTOFMS

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Using an optimized and validated GC×GC-HRTOFMS method we developed for the metabolic profiling of human serum, in combination with a strict QA/QC system, we were able to highlight sets of biomarkers capable to discriminate between various inflammation phenotypes (high, low, remission, and control) representatives of inflammatory bowel diseases. During this proof-of-concept study, two main challenges of untargeted metabolomics were especially considered.

First, the issue of data handling –large datasets and low number of samples compared to variables- was solved by the definition of a workflow of data preprocessing and processing, including the creation of a study template, the rigorous selection of good chromatographic quality features, and the multiplication of statistic techniques to be combined before test validation. In practice, 94 injections were made over 4 weeks, consisting of 70 study samples along with 16 QC samples and 8 reinjections due to QC system rejection. The all-chromatograms template included 524 verified features that were then reduced to less than two hundred after selection of the ones having an analytical variation under 30%, based on the QC samples. This resulted in the finding of robust biomarkers that positively discriminated between the different phenotypes of inflammation, including high and low inflammation, remission, and healthy statuses.

Second, the identification of unknown compounds was enhanced by using state-of-the-art high-resolution (HR) time-of-flight mass spectrometry and allowed to name and characterize putative biomarkers with higher degree of confidence.

In conclusion, this study showed the usefulness of optimized and fully controlled GC×GC-HRTOFMS in clinical research for proper biomarker identification. The collection of such data will also possibly contribute to biological pathways interpretation.

