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Microbial impact on bile acid metabolism in the disease state using UPLC-TMS

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Bile acid signatures can be used as indicators of metabolic status and of gut signaling and health. We detect these steroid molecules in different biological samples by UPLC-MS. Bile salts are conjugated bile acid (BA) moieties that are synthesized in the liver from cholesterol. They are now regarded as gut signaling hormones and are recognized as directing gene expression both locally and through cross-talk with the other tissues, mainly the liver. Following entry to the GI tract, microbial enzymes modify bile salts-bile salt hydrolase (BSH) enzymes and bile acids-bile acid inducible (Bai) enzymes in a spatial and temporal dependent manner. Hence, the gut microbiota is responsible for the range and the diversity of bile acids and salts and therefore microbial directed bile acid metabolism can play a central role in directing metabolic processes. While representatives of all the main phyla carry BSH, a property of gut associated bacteria only, these enzymes range in activity from none to very active and they show strain specific and different substrate specificities. Here, we present snapshot studies where we examine a range of bile acid altering activity in preclinical models of gut disease and in the disease state (Obesity, Short bowel Syndrome, Colitis) and their influence on host gene expression and gut health.

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The regulatory potential of protein post-translational modifications in chromatin biology and gene expression investigated by MS-based proteomics

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Chromatin is a highly dynamic, well-organized and yet ill-defined protein-DNA-RNA structure that controls various DNA-dependent processes. A large number of site-specific post-translational modifications of histones (hPTMs) contribute to the maintenance and modulation of chromatin plasticity, gene activation, DNA replication and repair and a variety of other biological processes and disease states. The observation of the diversity, frequency and co-occurrence of histone modifications at distinct genomic loci led to the notion that these marks create a molecular barcode, read by effector proteins that translate it into a specific transcriptional state, or process, on the underlying DNA. However, the molecular details of its working mechanisms are only partially characterized. More recently, various technological progresses have enabled the detection of these PTMs on an increasing number of non-histone proteins, involved in a variety of biological processes. Recent achievements made Mass Spectrometry (MS) and quantitative proteomics excellent tools to help understanding how histone and non-histonic PTMs mediate the structural-functional state of chromatin. My team contributed to the field by setting-up distinct MS-proteomics strategies, combined with various biochemical methods of enrichment of chromatin and extra-chromatin proteins, to investigate chromatin plasticity and nuclear dynamics governed by post-translational modifications. The talk will offer an overview of the MS-proteomics strategies developed to gain insights into chromatin biology, with emphasis on: The proteomic dissection of chromatin regulatory regions; the hPTMs-analysis of clinical specimens and the recent achievements on the methyl-proteome profiling and its impact in DDR and miRNA biogenesis

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