“Improving Metabolite Coverage in Untargeted LC-MS Metabolomics”

Résumé: The main objective of metabolomics/lipidomics is the analysis of all metabolites/lipids present in a particular biological system in order to study dynamic processes involved in an organism’s response to normal and abnormal biological or external stimuli. Metabolome effectively integrates both genetic and environmental inputs, thus providing the readout closest to the phenotype. This allows us to understand individual differences in response in unprecedented molecular detail. Mass spectrometry (MS) in combination with liquid chromatography (LC) is currently the most powerful technique to use for untargeted metabolomics because it provides the highest metabolite coverage in a single analysis. However, current gold standard protocols are capable of detecting only medium to high abundance metabolites, often yielding no information on biologically-important metabolites present in low concentrations. Furthermore, standard untargeted metabolomics protocols do not provide accurate information for unstable metabolites leading to erroneous biological interpretation due to analytical artefacts. My research program focuses on resolving some of these major challenges in current metabolomics analysis of biological fluids and tissues by: (i) increasing accuracy and metabolome coverage of low abundance metabolome, and (ii) improving analysis of unstable metabolome such as eicosanoids and lipid peroxidation products. In this talk, I will discuss different sample preparation strategies that can be used to improve metabolome coverage in global metabolomics approaches including sequential extraction and new extraction materials such as nanomaterials and ionic liquids. I will also discuss briefly the important role that the mobile phase additives can play to improve electrospray ionization (ESI) efficiency, with particular focus on the usefulness of acetic acid mobile phase additives for negative ESI. In particular, I will show the advantages of using this mobile phase to improve lipid coverage for untargeted lipidomics in plasma. Finally, I will briefly discuss in vivo solid-phase microextraction as a new technique for measuring lipidome in live, freely moving animals for the first time.