Metabolomics for food and environmental toxicology : from targeted to global integrative approaches

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Man is daily exposed to numerous chemical compounds, present in mixtures at low doses in the food and the environment. The assessment of the risk associated to this chronic exposure requires to be able to determine trace contaminants within complex matrices in order to look at exposures parameters, and to develop analytical strategies covering from specific spectrometric approaches for the identification of the contaminant metabolic pathways to global metabolomic approaches for studying their impact on the general metabolism and metabolic networks.

In this presentation, some examples illustrating the use of LC-MS based metabolomic approaches in the frame of metabolomic studies conducted in our laboratory will be given. In a first example, the development of a method using LC coupled to high resolution MS for the non targeted screening of aldehydic compounds produced by lipid peroxidation will be presented. The use of this method for the detection and characterization of putatively new luminal aldehydes (particularly the reactive alkenals) will be presented. A second example will describe the use of both targeted and non-targeted methods for studying the fate and the effects of the endocrine disruptor Bisphenol A from both *in vivo* and *in vitro* approaches. On the one hand, a targeted method has been developed, allowing the identification and measurement of Bisphenol A and its main metabolites as biomarkers of exposure. On the other hand, a global LC-HRMS method has been developed and applied to the study of the effects of exposure to low doses of Bisphenol A at the cellular level (HepaRG cells). Cellular extracts have been analyzed using LC-ESI-HRMS in both positive and negative modes. After reduction using both XCMS and a home-made interface, data were treated using multivariate statistical tools (PCA, PLS-DA). A pipeline is now being constructed for the in-depth study of the metabolic network of HepaRG cell models and its disruption by chemicals, using the produced LC-HRMS data for the inference of the network.

These examples clearly show the increasing role of LC-MS based metabolomics in the field of food and environmental toxicology by allowing to access to quantitative external or internal exposure data, identification of biomarkers of effects, and also to information on the mechanism of action of toxic contaminants.