

## **Metabolomics for the study of xenobiotic metabolism and toxicity**

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Metabolomics is the study of changes in the population of small molecules or metabolites, in cells, tissues and biological fluids such as serum and urine. Metabolomics, using  $^1\text{H-NMR}$ , has gained prominence and been embraced by the pharmaceutical industry as a means to determine the potential toxic effects of drugs. For example, a chemical is administered to rodents and urine and serum examined for the presence of metabolites that reflect organ-specific toxicities. Humans can also be examined during clinical trials for the presence of biomarkers for toxicity. More recently, mass spectrometry coupled with liquid or gas chromatography, is gaining increased use for metabolomics due to high resolution, lower costs and more widespread equipment availability as compared to NMR. In particular, ultra performance liquid chromatography coupled with time-of-flight mass spectrometry (UPLC- TOFMS) yields high-resolution separation and exact mass determination of compounds in biological materials. The UPLC-TOFMS data are deconvoluted by various chemometric data analysis (CDA) software such as principal components analysis (PCA) to find differences between samples. To study xenobiotic metabolism and toxicity, compounds are administered to mice and serum and urine examined by PCA for the presence of the parent compound and its metabolites that are not found in untreated mice. Metabolites derived from the drug as well as endogenous metabolites that reflect the drug's biological activity or toxicity can be resolved. Metabolomics is also being used to search for biomarkers for various diseases that involve chemical insults. Compounds are administered to mice and tissues, serum and urine are examined for the appearance of biomarkers that reflect toxicity and inflammation. These biomarkers can also be of value to determine the mechanism of toxicities. Examples of recent studies using the common analgesic acetaminophen (paracetamol) will be presented.