Metabolomic Analysis of Rat Urine Following Acute Exposure to Perfluorinated Chemicals

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Perfluorinated chemicals (PFCs), namely perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), represent an emerging class of persistent and bioaccumulative compounds. Global occurrence of these fluorochemicals, coupled with probable human exposure, has prompted investigations of the biochemical impacts of PFCs that elicit toxicity through modulation of peroxisome proliferator-activated receptors (PPAR) as well as other modes of action. Genomic studies have shown that PFOA and PFOS affect genes involved in cholesterol synthesis and fatty acid metabolism and result in signs of steatosis and hepatomegaly in rats. As a biomarker-based approach, this study focused on the use of metabolomics for identifying fluxes in the endogenous metabolome using proton nuclear magnetic resonance (^{1}H-NMR) and both liquid and gas chromatography coupled to mass spectrometry (LC-MS^n and GC-MS). To study this, male SD rats were dosed daily by gavage for 5 days with 20 mg/kg PFOA or 10 mg/kg PFOS. Urine was collected 24 hrs prior to, and twice daily during, the exposure period at 8 and 16 hr intervals. Urine was either buffered (^{1}H-NMR), filtered and diluted (LC-MS^n), or extracted with chloroform:methanol, lyophilized and derivatized (GC-MS) prior to analysis. Spectra were subjected to principal components (PCA) and partial least squares discriminant analysis (PLS-DA) to determine the effects of each PFC on the urinary metabolite profile. For each analytical platform, differences between the control and exposed rats were observed at the earliest time point. Moreover, PFC-related effects were temporal and classes sustained distinct separation following three days of exposure. Components of the spectra responsible for time and PFC-dependent clustering are being investigated. Identification of significant changes in urinary metabolites will aid in identifying biomarkers associated with PPAR activation, hepatotoxicity, and exposure to these and other PFCs.