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# Metabolomics and transcriptomics analyses of Acetaminophen and Carbon Tetrachloride induced hepatotoxicity

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Drug-induced liver injury (DILI) is the leading cause of drug failure. The prevalence of serious adverse effects is due in part to inefficient and inaccurate biomarkers of toxicity in preclinical studies. ALT and BILI are the commonly measured parameters to assess liver injury. However, ALT elevation can occur without signs of liver injury so it not specific enough. BILI only elevates upon severe liver damage. Therefore, there is a need for more specific biomarkers of liver injury and dysfunction. The omics methods have the potential to detect early biomarkers of toxicity in biofluid samples. In an effort to identify biomarkers of DILI, metabolomics and transcriptomics data were acquired on urine and serum samples in two separate studies. In the first study, Sprague Dawley rats were dosed with 0, 100 or 1250 mg acetaminophen (APAP)/kg body weight. Urine, serum, and tissue were collected 6 hr, 1 d, 3 d, and 7 d post-dosing. Metabolites in pathways involving oxidative stress, bile acids, and lipid ketones were altered. The transcriptomics data indicated genes within the same pathways were altered. In the second study, rats were dosed with 0, 50, or 2000 mg carbon tetrachloride ($CCl_4$)/kg body weight and samples collected 6 hr, 1 d, and 3 d post-dosing. Similar to the results in the APAP study, metabolites and genes involved in oxidative stress, bile acids, and lipid ketones were altered. The arginine metabolism and glycolysis pathways were also affected following administration of $CCl_4$. Omics technologies can provide potential new biomarkers and pathway information.

## Biography

Laura Schnackenberg received her Ph.D. in Analytical Chemistry from the University of North Carolina at Chapel Hill and held a postdoctoral fellowship at the National Center for Toxicological Research (NCTR). She is currently a Research Chemist in the Center for Metabolomics within the Division of Systems Biology at NCTR. She has co-authored more than 30 manuscripts in peer reviewed journals including several expert reviews on the use of metabolomics in biomarker discovery and as a tool for personalized medicine.