The Metabolomics Workflow for Nutritional Pharmacology/Toxicology

The Metabolomics and Exposome Laboratory (MEL) at the Nutrition Research Institute (NRI) is using untargeted metabolomics/exposome approaches to reveal pharmacological and nutritional targets for development of Intervention Strategies. Contact Us to Collaborate!

**Research Questions:** Whether a study is looking at treated vs untreated, high vs low dose, cases versus controls, or responders vs non-responders, untargeted metabolomics can be a powerful tool to interrogate mechanisms of a therapeutic/toxin, or discover drug or nutritional targets for a disease. The MEL takes extracts of cells, tissues, or biological fluids from *in vivo* or *in vitro* studies and subjects them to untargeted metabolomics analysis. The metabolomics data is analyzed using phenotypic anchors obtained from tissue culture studies (e.g., LDH, glucose), or from studies with *in vivo* models or human subjects (e.g., health status, dietary intake, medications, clinical chemistries). Other factors that may be included in modelling include genetic variants, protein expression, microbial populations, lifestyle factors, etc. This allows researchers to uncover the role of metabolism in their studies, generating exciting new hypotheses for future studies. This approach is applicable to studying diseases or dysfunctions across the lifespan including cancer, pregnancy/birth outcomes, hypertensive disorders, diabetes, neurological disorders, addiction, microbiome-related processes, and more.

**Analytical Approach:** We conduct metabolomics research using UHPLC Q-Exacte HFx Mass Spectrometers. Our method detects tens of thousands of signals for molecules that are present in relatively non-invasive biological fluids (e.g., urine, serum, plasma), and extracts of cells and tissues (e.g., liver, brain, placenta, stool, cecum). Detectable analytes have been established via an in-house physical standards library of RT, exact MS, and MS/MS fragmentation for endogenous and exogenous metabolites of the host system, microbial metabolism, exposures (e.g., nicotine, illicit drugs, environmental compounds), treatments (e.g., medications, supplements, natural products), and dietary intake (e.g., nutrients, vitamins, components of foods). Big data analytics against external public databases (e.g., HMDB) are also used to annotate signals.

**Computational Approaches:** An overarching goal of these analyses include discovering pharmacological and nutritional targets and proposing intervention strategies. Univariate and multivariate statistics are conducted using SAS, JMP, and SIMCA. Linear and logistic regression models are used to determine signals that define study phenotypes. Biological significance is revealed through pathway mapping.

**Example Publications**