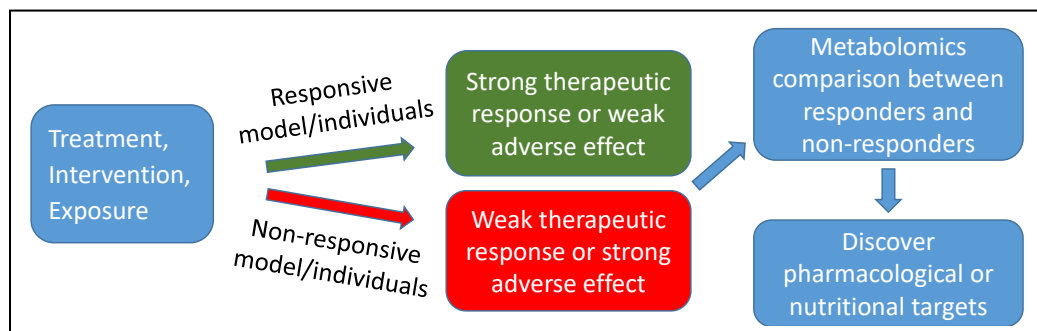


The Metabolomics Workflow for Nutritional Pharmacology/Toxicology

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-Exactive 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

- Could Nutrient Cocktails play a role in diminishing addiction and reducing adverse side effects of substance abuse? <https://sph.unc.edu/sph-news/could-nutrient-cocktails-play-a-role-in-diminishing-addiction-reducing-adverse-effects-of-substance-abuse/>
- Ghanbari, R., Li, Y.-Y., Pathmasiri, W et al., 2021. Metabolomics Reveals Biomarkers of Opioid Use Disorder. *Translational Psychiatry*, 11(1) p. 103. doi: 10.1038/s41398-021-01228-7 PMID: 33542199
- Li, Ghanbari, et al., 2020. Untargeted Metabolomics: Biochemical Perturbations in Golestan Cohort Study Opium Users Inform Intervention Strategies. *Front Nutr*, 7, p. 584585. eCollection 2020. PMID: 33415121.
- Rushing, BR et al., 2021. Fecal Metabolomics Reveals Products of Dysregulated Proteolysis and Altered Microbial Metabolism. *Osteoarthritis and Cartilage*. (Submitted).
- Li, Y-Y et al., 2019. A Metabolomics Approach to Investigate Kukoamine B-A Potent Natural Product With Anti-diabetic Properties. *Front Pharmacol*. doi: 10.3389/fphar.2018.01575
- Li, Shuang, et al. 2021. Multi-omics analysis of glucose-mediated signaling by a moonlighting Gβ protein Asc1/RACK1. *PLoS Genetics* (Submitted).

Interested in Nutritional Pharma/Tox? Contact Us!	
Contact	Email/Phone
Yuanyuan Li, PhD Assistant Professor, NRI Dietary Exposome	yuanyli4@unc.edu 704-250-5000
Blake Rushing, PhD Assistant Professor, NRI Pharmacology	Blake_rusing@unc.edu 704-250-5000
Susan Sumner, PhD Professor of Nutrition Director, MEL at the NRI	Susan_sumner@unc.edu 919-622-4456