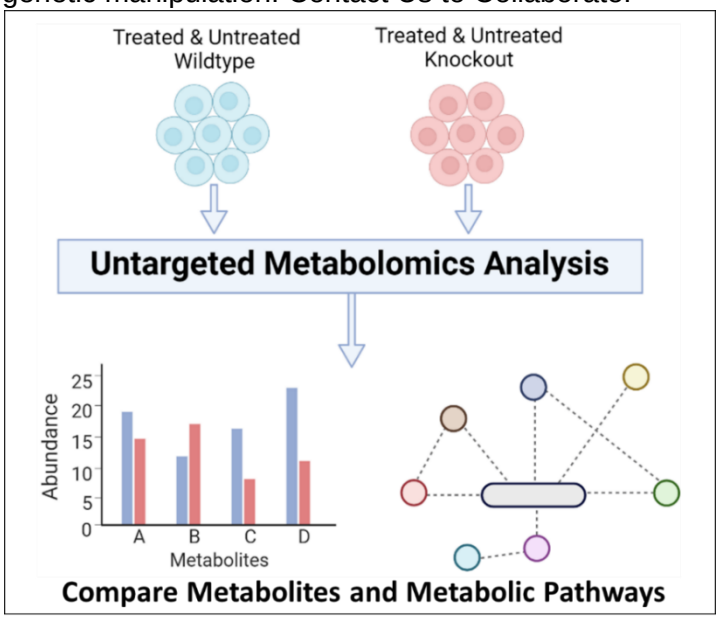
Metabolomics: Using In Vitro Models to Reveal Mechanisms of Cellular Response

The Metabolomics and Exposome Laboratory (MEL) at the Nutrition Research Institute (NRI) is using untargeted metabolomics/exposome approaches to reveal the metabolic response of cells to treatment or genetic manipulation. Contact Us to Collaborate!



Research Questions: Metabotyping *in vitro* models provides a powerful approach to examine mechanisms of cellular response to drug, toxin, or nutrient exposure, and discover important genes and proteins. Metabolomics studies are designed to compare treated and untreated cells derived from cell models, including knockout and wildtype systems. Untargeted metabolomics can reveal biochemical underpinnings that lead to phenotypic differences or treatment response. The MEL extracts cells and media, and captures data using high resolution mass spectrometry and NMR spectroscopy.

Comparisons are made between study groups, such as treated vs untreated or wildtype vs knockout. Other factors that may be included in these comparisons are protein expression, morphological differences, treatment sensitivity/resistance, proliferation rate, migration rate, etc. This approach allows researchers to uncover the role of metabolism in their studies, generating exciting new hypotheses for future projects.

Analytical Approach: We conduct metabolomics research using UHPLC Q-Exactive HFx Mass Spectrometers, and NMR Spectroscopy. Our method detects tens of thousands of signals for molecules that are present in extracts of cells or secreted in culture medium. The range of analytes detected have been established via an in-house physical standards library of RT, exact MS, and MS/MS fragmentation for many classes of metabolites in eukaryotic or prokaryotic systems. Big data analytics against external public databases (e.g., NIST, HMDB) are also used to further annotate signals with named metabolites. Isotopic labels are incorporated to monitor metabolic flux through pathways.

Computational Approaches:
An overarching goal of these analysis include discovering novel pharmacological/nutritional targets and propose intervention strategies against disease. Univariate and multivariate statistical analysis are conducted using SAS, JMP, and SIMCA, and data are used in linear and logistic regression models to determine signals that define study phenotypes. Biological significance is further revealed through pathway mapping.

Interested in Cell Metabolomics Analysis? Contact Us!

Contact	Email/Phone
Blake Rushing, PhD Assistant Professor of Nutrition MEL at the NRI	Blake_rushing@unc.edu 704-250-5000
Susan Sumner, PhD Professor of Nutrition Director, MEL at the NRI	Susan_sumner@unc.edu 919-622-4456

Example Publications

- Li, S., Li, Y., Rushing, B.R., Harris, S.E., McRitchie, S.L., Jones, J.C., Dominguez, D., Sumner, S.J. and Dohlman, H.G., 2021. Multi-omics analysis of glucose-mediated signaling by a moonlighting Gβ protein Asc1/RACK1. PLoS genetics, 17(7), p.e1009640.
- Li, Y.Y., Douillet, C., Huang, M., Beck, R., Sumner, S.J. and Styblo, M., 2020. Exposure to inorganic arsenic and its methylated metabolites alters metabolomics profiles in INS-1 832/13 insulinoma cells and isolated pancreatic islets. Archives of toxicology, 94(6), pp.1955-1972.
- Stewart, D.A., Winnike, J.H., McRitchie, S.L., Clark, R.F., Pathmasiri, W.W. and Sumner, S.J., 2016. Metabolomics analysis of hormone-responsive and triple-negative breast cancer cell responses to paclitaxel identify key metabolic differences. Journal of proteome research, 15(9), pp.3225-3240.

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