UNIVERSITY OF LOUISVILLE

COLLEGE OF ARTS & SCIENCES

Department of Chemistry

Brown and Williamson Series

Friday, April 23, 2021
@12:30 pm
Via: MS TEAMS

Haiwei Gu, Ph.D.

Assistant Professor,
College of Health Solutions,
Arizona State University

Development and Applications of Advanced Targeted Mass Spectrometry in Metabolomics

ABSTRACT:

Metabolic flux analysis (MFA) using stable isotope labeled tracers is highly relevant to understanding metabolic mechanisms of various biological processes. While the pace of methodology development in MFA has been rapid, a major challenge the field continues to witness is limited metabolite coverage, often restricted to a small to moderate number of well-known compounds. In addition, isotopic peaks from a metabolite tend to dramatically decrease with m/z, which makes liquid chromatography tandem mass spectrometry (LC-MS/MS) highly useful in MFA due to its high sensitivity and specificity. Previously we have built large-scale LC-MS/MS approaches that can be routinely used for measurement of up to ~1,900 metabolite levels. In this study, we expanded our previous studies focused on metabolite level measurements to flux analysis and established a novel comprehensive isotopic targeted mass spectrometry (CIT-MS) method for reliable MFA analysis with broad coverage. CIT-MS is operationalized using multiple reaction monitoring (MRM) mode and is able to perform MFA of 310 identified metabolites selected from >35 metabolic pathways of strong biological significance. As a proof-of-principle, we have applied CIT-MS to compare the steady-state enrichment of metabolites between Myc(oncogene)-on and Myc-off Tet21 human neuroblastoma cells cultured with U-13C6-glucose medium. Further, we developed a novel concept of relative flux, which eliminates the requirement of absolute quantitation in traditional MFA and thus enables comparative MFA under the pseudosteady state. As a result, CIT-MS was shown to possess the advantages of broad coverage, easy implementation, fast throughput, and more importantly, high fidelity and accuracy in MFA. In principle, CIT-MS can be easily adapted to track the flux of other labeled tracers (such as 15N-tracers) and in various biological models (such as mice). Therefore, CIT-MS has great potential to bring new insights to both basic and clinical metabolism research.

BIO:

Dr. Haiwei Gu obtained his Ph.D. degree from Purdue University, under the supervision of Dr. Daniel Raftery (2003-2008). Dr. Gu received his postdoctoral training focused on LCxLC, with Dr. Peter Carr in the University of Minnesota. From 2011-2017, Dr. Gu worked as a Research Assistant Professor working in the Northwest Metabolomics Research Center (NW-MRC) directed by Dr. Raftery in the University of Washington. Currently, Dr. Gu is an Assistant Professor in the College of Health Solutions, Arizona State University. Metabolomics research in the Gu Lab has focused on the development of advanced analytical tools and statistical methodologies for profiling metabolites and metabolic pathways in complex biological systems, and their applications to study diseases, nutrition, drug toxicity, environment, etc. Dr. Gu has published >90 peer-reviewed articles, with an h-index of 34. Dr. Gu has also served the community as a member in editorial boards of Current Metabolomics and Metabolites, and as an ad-hoc reviewer for journals such as Analytical Chemistry, Journal of Proteome Research, etc.