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Development of a Multi-faceted Mass Spectrometry-based Platform for Neuroscience and Biomedical Research

ABSTRACT: Comprehensive characterization of all signaling molecules in a nervous system with chemical, spatial and temporal information is often critical to deciphering the functionality of a neural circuit yet it presents a daunting challenge. In this presentation, I will present our recent progress on the development of a multi-faceted mass spectrometry (MS)-based analytical platform to probe neuronal signaling with enhanced sensitivity and selectivity. By combining chemical labeling, micro-scale separation, and tandem MS sequencing techniques, we discovered more than 300 novel neuropeptides in crustacean nervous systems and explored peptidomic changes in feeding using both crustacean and mammalian model organisms. Moreover, both mass spectrometric imaging (MSI) technology and *in vivo* microdialysis sampling tools have been developed and implemented to follow neuropeptide distribution and secretion with unprecedented details. Furthermore, novel dimethylated leucine (DiLeu) isobaric tagging reagents have been developed and employed to offer cost-effective implementations that enable higher order of multiplexing. Additionally, we report on a multiplexed quantitation method for simultaneous proteomics and amine metabolomics analyses via nanoflow reversed phase LC-MS/MS, exploiting mass defect-based DiLeu (mdDiLeu) labeling. Several on-going efforts and future perspectives provided by these enabling technologies will be highlighted and discussed.

BIO: Dr. Lingjun Li is a Vilas Distinguished Achievement Professor and the Charles Melbourne Johnson Distinguished Chair Professor of Pharmaceutical Sciences and Chemistry at the University of Wisconsin-Madison (UW-Madison). Dr. Li received her Ph.D. degree in Analytical Chemistry/Biomolecular Chemistry from the University of Illinois at Urbana-Champaign under Jonathan Sweedler in 2000. She then did joint postdoctoral research at the Pacific Northwest National Laboratory (w/ Richard Smith) and Brandeis University (w/ Eve Marder) before joining the faculty at UW-Madison in December 2002. Dr. Li's research interests include the development of novel mass spectrometry (MS)-based tools such as new isotopic and isobaric labeling strategies that enable hyperplexing for quantitative proteomics, peptidomics, and glycomics. She and her team also develop microscale separations, *in vivo* microdialysis and imaging MS tools for functional discovery of neuropeptides in model organisms and (glyco)protein biomarkers in neurodegenerative diseases. Her lab also explores novel use of ion mobility MS to address technical challenges in peptidomic research, including site-specific peptide epimer analysis and improvement of isobaric tandem MS quantitation. Professor Li has established a highly productive research program and published more than 270 peer-reviewed research journal papers and has given more than 200 invited talks. She has successfully graduated 46 PhDs and is currently training 21 PhD graduate students and 6 postdoctoral scientists. She has been recognized with numerous awards, including ASMS Research Award, NSF CAREER Award, Sloan Fellowship, PittCon Achievement Award, and ASMS Biemann Medal, and was named one of the Top 50 most influential women in the analytical sciences and was included in the 2016 Analytical Scientist Power List. Dr. Li is currently serving as an Associate Editor for the *Journal of the American Society for Mass Spectrometry (JASMS).*