Department of Biomedical Engineering
UNIVERSITY OF WISCONSIN–MADISON

Fall 2023 Seminar Series

Kinase assay tool development using mass spectrometry and fluorescence lifetime imaging

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Protein phosphorylation is a crucial post-translational modification in all cells, carried out by kinase enzymes and reversed by phosphatase enzymes. It is regulated by a broad range of factors including protein-ligand and protein-protein interactions, scaffolding, and subcellular localization. Dysregulation of kinase activity leads to cellular abnormalities and disease, and thus kinases are a key target for drug discovery. Most assays to detect kinase activity are either endpoint-based and/or require lysis of cells (which loses contextual information), or require genetically encoded sensors in engineered cellular systems. We have used phosphoproteomics and AI-based structural modeling to determine substrate preferences and design novel synthetic, kinase substrate sequences. We have also linked fluorophore-labeled versions to cell penetrating peptides, delivering peptide-based biosensors to live cells and mapping more than one subcellular kinase activity at a time via fluorescence lifetime imaging microscopy. Overall, we show how synthetic peptides can be used in vitro and in cells to detect dynamic kinase activity to better evaluate inhibitor pharmacology and/or understand target kinase biology in a more biologically-relevant system than in recombinant assays.

ABOUT the SPEAKER

Laurie Parker is a Professor in the Biochemistry, Molecular Biology and Biophysics Department at the University of Minnesota Twin Cities. She did her PhD at the University of Glasgow in Scotland in Synthetic Organic Chemistry, and postdoc training at the University of Chicago in chemical biology and proteomics. Bringing this interdisciplinary background to her research, her lab works on understanding kinase substrate preferences in order to design more pharmacologically-relevant assays and detection approaches for inhibitor drug discovery and target validation, using peptide chemical biology, mass spectrometry/proteomics, and fluorescence spectroscopy including fluorescence lifetime-based detection.

Monday, October 16 at Noon
1003 Engineering Centers (Tong Auditorium)