School of Molecular Sciences
Arizona State University

SMS Spring 2022 Seminar Series

Friday Jan 21 | 2:30pm | Virtual*

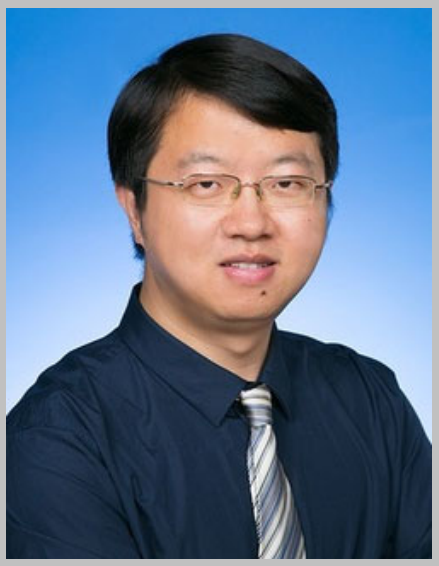
Interrogating Disease-related Protein-Protein Interactions with Fluorine-Thiol Displacement Reactions (FTDRs)

ProteinsPost-translational modifications (PTMs) modify existing proteins with additional chemical functionalities, resulting in the mediation of signaling events underlying various cellular processes. The dysregulation of PTMs has been closely related to the onset and/or relapse of human diseases. Yet, many PTM-related non-histone proteins and enzymes remain to be elucidated in terms of their identity, functions, and roles in cellular activities such as activation, proliferation, and migration, simply due to the lack of tools for characterization.2 Despite the development of bioorthogonal chemical reactions such as "click chemistry", few research programs have explored protein labeling or tagging with reduced sterics. Towards this end, my group has invented a steric-free bioorthogonal reaction (fluorine-thiol displacement (FTDR))1 and has developed a novel class of FTDR-based imaging and proteomics probes aimed at a complete dissection of substrate proteins of acetylation that are featured in diseased cells such as cancer cell lines; which for now cannot be systematically profiled due to limitations in the current chemical proteomics approach that heavily relies on sterically hindered 'click chemistry' tags.1 Using quantitative proteomics in tandem with FTDR labeling, we have recently identified 92 new protein substrates of acetylation in prostate PC3 cells and are validating their roles in PC3 cell proliferation and migration.

Concurrently, to facilitate the studying and targeting of any new protein-protein interactions (PPIs) to be revealed by the aforementioned research investigations in PTM signaling, we also exploited other tool probes3-4 such as peptide stapling4 based on the FTDR reaction. The resulting peptides possessed improved folding, stability, and on-target affinity, but also displayed enhanced cell penetration than the peptides stapled by traditionally used ring-closing metathesis.4 As an on-going effort, my group has been applying this peptide stapling to interrogate Axin-β-catenin interactions and p53-MDM2 interactions that are key to the onset and relapse of breast cancers, leukemia, and lymphoma, etc, as well as PPIs of protein tyrosine phosphatases that are important to neuron regeneration.

Rongsheng (Ross) Wang, PhD

Assistant Professor, Temple University



Rongsheng (Ross) Wang is an Assistant Professor of Chemistry at Temple University. Ross obtained his under-graduate degree in bioinorganic chemistry from Nanjing University (NJU), China, between 2001 and 2005. From 2005, Ross joined the Ph.D. program in bioorganic chemistry at Washington University in St Louis (WUSTL). His thesis work with Prof. John-Stephen Taylor focused on the development and study of small molecule/peptide-based inhibitors and probes of heat shock protein 70. From 2010 to 2012, Ross spent a short spell at a local biotech company, Mediomics, LLC, to invent protein or aptamer -based fluorescence sensors that enables homogeneous rapid detection of biomarkers. In 2012, Ross joined the laboratory of Prof. Peter G. Schultz as a postdoctoral research fellow at the Scripps Research Institute (TSRI). In the postdoctoral work period, Ross was engaged in inventing a new generation of site-specific antibody drug conjugates for treating inflammatory disorders. He was also actively involved in the discovering of a protein engineering platform that can generate functional antibodies to serve as the first-in-class selective therapeutics for cancer and autoimmune diseases. From July 2016, Ross started his independent research career at Temple University. The focus of his current research is the invention of bioorthogonal chemical reactions and the development of various chemical biological tools, which allow us to interrogate complex biological systems and to develop novel therapeutics. He has been recognized by American Cancer Society IRG Award (ACS), Leukemia SPORE Career Enhancement Award (MD Anderson), Scialog Fellow (Research Corporation), Chemical Machinery of the Cell Collaborative Innovation Award (Gordon & Betty Moore Foundation), Cottrell Scholar Award (Research Corporation), NSF CAREER Award, and the R35 Maximizing Investigator's Research Award from NIH.

**ZOOM: https://asu.zoom.us/j/87081218152*