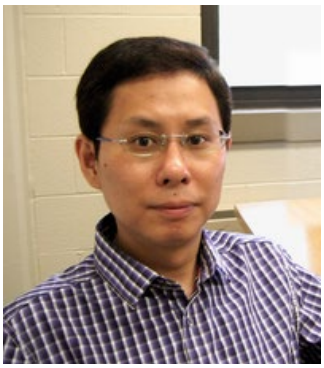
Department of Biochemistry and Molecular Biophysics Seminar

Wednesday, September 9 at 4:00 p.m. in Ackert 120

Coffee and cookies at 3:45 p.m. in Chalmers 168



Dr. Ping Li, University Outstanding Scholar, Associate Professor, and Director of Protein and Biopolymer Analysis Core Lab

Department of Biochemistry and Molecular Biophysics
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Chemical Insight, Biological Impact: From Molecular Probes to Engineered Biocatalysts

My chemical biology program uses molecular probes and mechanistic enzymology to reveal how chemical modifications and heme catalysis shape biological function, then converts those insights into selective perturbation and catalyst design. The NTMT1 program addresses N-terminal methylation, an understudied protein mark linked to chromatin organization, DNA repair, mitosis, translation, development, aging, and context-dependent cancer phenotypes. To discover physiological substrates, we combined Hey-SAM labeling, click chemistry, affinity enrichment, and LC-MS/MS proteomics, identifying 72 candidate NTMT1 targets and validating OLA1 methylation in cells. We then developed the first reported selective cellular NTMT1 degrader, which achieved a DC_{50} of 7.53 μM and > 90% maximal degradation in HCT116 cells while sparing NTMT2. Label-free global MS proteomics further revealed calreticulin upregulation, and complementary cancer models showed growth inhibition and G0/G1 arrest. The DyP program asks how H_2O_2-driven heme chemistry can be decoded and engineered for lignin valorization, dye oxidation, and new-to-nature catalysis. In *Tc*DyP, structural and radical-trapping studies identified Trp263 as a substrate-oxidation site and Trp376 as an off-pathway radical sink. *El*DyP studies revealed a water-ligated heme, dual access channels, Asp143-dependent cmpd 0 deprotonation, mechanistically important *aquo* release, and a turnover-limiting conformational reset. DyPB instead relies strongly on Arg244 for cmpd I formation and Asp153 for reduction, with a wet cmpd I undergoing sequential one-electron steps. Ir(Me) incorporation endows *Tc*DyP with new catalytic activity. Together, these studies show how chemistry can map hidden biology, create selective cellular probes, and define engineering levers for controlling electron flow, substrate scope, oxidative efficiency, and future artificial metalloenzymes across biomedicine and biocatalysis.