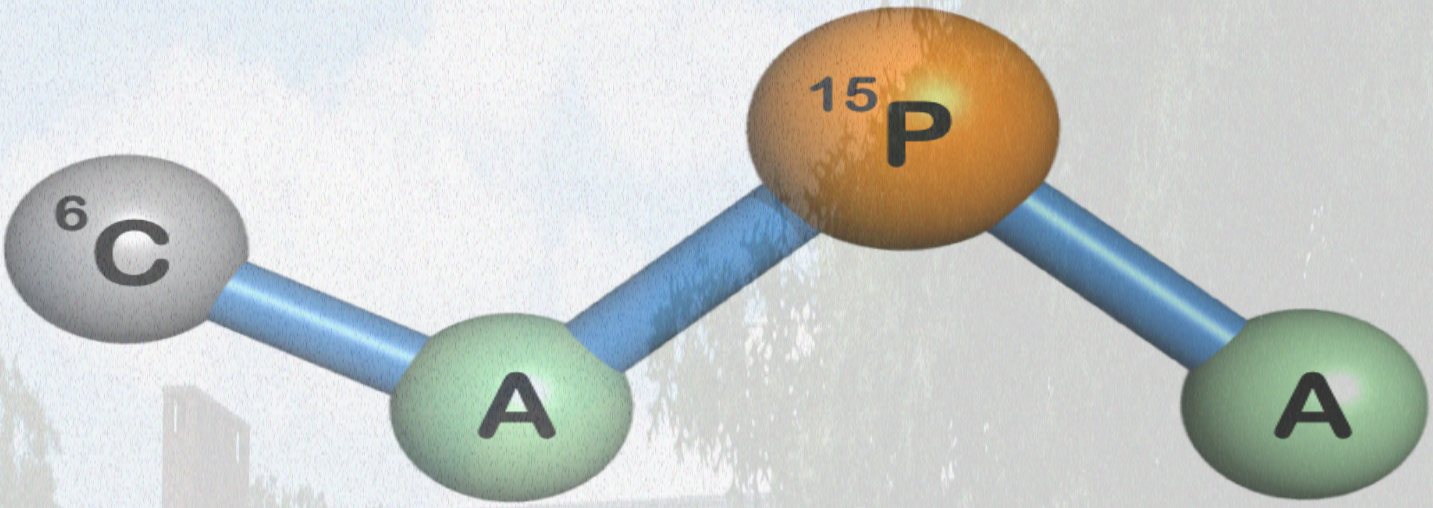


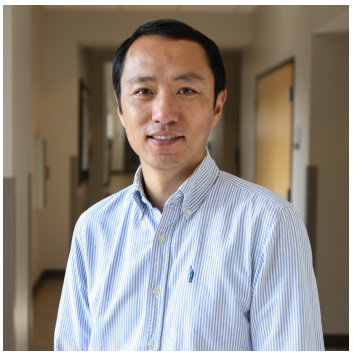
Chinese American Chemistry & Chemical Biology Professors Associations

CAPA 2025 Fall Symposium

August 17, 2025

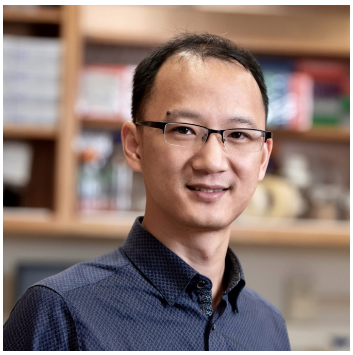
@ University of Maryland College Park

Invited Speakers



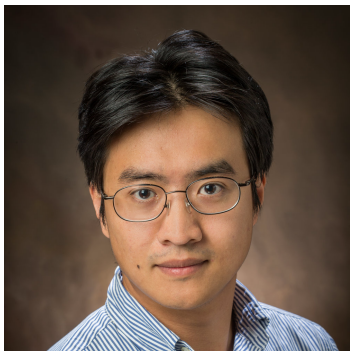
Chen, Ming
Virginia Tech

Diao, Tianning
New York University

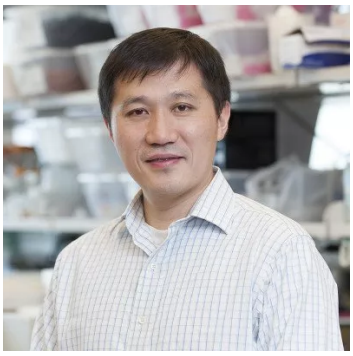


Huang, Xiongyi
John Hopskins University

Li, Lei
Georgia State University

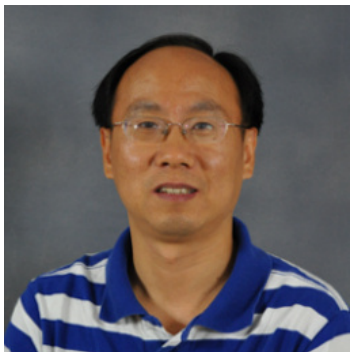


Liu, Wei
Virginia Tech



Luo, Minkui
Sloan Kettering Cancer Center

Sun, Wenfang
University of Alabama

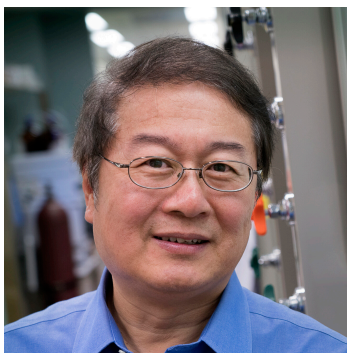


Tang, Chuanbing
University of South Carolina

Wang, Binghe
Georgia State University

Wang, Qian
University of South Carolina

Yang, Zhongyue
Vanderbilt University



Zhang, Zhong-Yin
Purdue University

Symposium Schedule

Time	Speaker		Chair
9:00-9:05	Opening Ceremony		
9:05-9:30	Liu, Wei Virginia Tech	*High-Valent Copper in Catalysis*	Qian Wang
9:30-9:55	Zhongyue John Yang Vanderbilt University	*Physics-Guided Protein Engineering*	
9:55-10:20	Luo, Minkui Sloan Kettering Cancer Center	*Assembling Ternary Dead-end Complexes for Covalent Trapping of Epigenetic Modulators of Protein Methylation*	
10:20-10:30	Coffee break		
10:30-10:55	Zhang, Zhong-Yin Purdue University	*Advancing Drug Discovery by Targeting Protein Tyrosine Phosphatases*	Ross Wang
10:55-11:20	Diao, Tianning New York University	*Nickel-Catalyzed Suzuki-Miyaura Coupling of Heteroaromatic Molecules for Process Synthesis*	
11:20-11:45	Wang, Qian University of South Carolina	*Cyclopropanols as Biorthogonal Warheads for Bioconjugation and Biomedical Applications*	
11:45-12:00	Sponsor talks		
12:00-1:00	Lunch Break		
1:00-1:25	Chen, Ming Virginia Tech	*Catalytic Transformations of Organoboron Compounds*	Zhong-Yin Zhang
1:25-1:50	Sun, Wenfang University of Alabama	*Near-Infrared Ir(III) and Ru(II) Complexes: Photophysics and Applications for Phototherapy*	
1:50-2:15	Wang, Binghe Georgia State University	*Reactive Oxygen Species Research: Guardrails against Data Inconsistencies and Mis-Interpretations*	
2:15-2:30	Coffee break		
2:30-2:55	Li, Lei Georgia State University	*Chemoenzymatic Strategies to Expand the Synthetic Glycome*	Binghe Wang
2:55-3:20	Huang, Xiongyi John Hopskins University	*Unlocking New Possibilities in Enzymatic Transition Metal Catalysis*	
3:20-3:45	Tang, Chuanbing University of South Carolina	*Designing Facial Amphiphilicity for Fighting Multidrug-Resistant Bacteria*	
3:45-4:00	Closing Ceremony/Picture taking		
4:00-5:00	Transportation		
5:00-10:00	CAPA Annual Reception		

Catalytic Transformations of Organoboron Compounds

Ming Chen

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We focus on the development of catalytic transformations of organoboron compounds. One area we have been working on is the Cu-catalyzed asymmetric functionalization of 1,3-dienylboroates. By using boryl anion effect, 1,3-dienylboroates can be converted into ketones and tertiary alcohols with excellent regio-, stereo-, and enantioselectivities. The methods have been successfully applied to complex molecule synthesis. DFT studies were conducted to interrogate the origins of observed selectivities. More recently, we have been working on radical chemistry with organoboron compounds. Under photochemical conditions, alkyl boronates can undergo radical-based transformations to generate synthetically valuable products.

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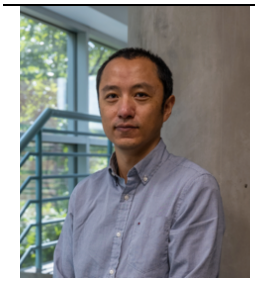

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Nickel-Catalyzed Suzuki-Miyaura Coupling of Heteroaromatic Molecules for Process Synthesis

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The synthesis of active pharmaceutical ingredients (APIs) containing heteroaromatic motifs often relies on palladium-catalyzed Suzuki-Miyaura coupling (Pd-SMC), a transformation that can account for a significant portion of the production costs for small-molecule drugs. Nickel-catalyzed SMC offers a more economical and sustainable alternative, but its implementation on scale has been hindered by high catalyst loadings and a limited scope of heterocyclic coupling partners. We introduce a family of (ProPhos)Ni catalysts that enable efficient and robust Ni-SMC of heterocycles. ProPhos ligands feature a phosphine moiety tethered to a hydroxyl group, which facilitates transmetalation and improves catalyst stability. The (ProPhos)Ni catalysts accommodate a wide range of heteroaromatic core structures, including those present in commercial APIs, with catalyst loadings of 0.1-0.5 mol%. The (ProPhos)Ni-SMC has been successfully validated on decagram scale and represents a versatile platform with significant potential for adoption in commercial process synthesis.

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Unlocking New Possibilities in Enzymatic Transition Metal Catalysis

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Repurposing natural enzymes to catalyze synthetic transformations absent in nature has emerged as a significant research field bridging chemistry and biology. A key challenge in this pursuit is the introduction of synthetic reaction mechanisms into natural protein scaffolds. Over the past decades, substantial breakthroughs have been achieved in this field, with many enzymatic systems developed to catalyze critical chemical transformations not previously observed in biology. However, much of this progress has focused on proteins or enzymes containing heme or organic cofactors. In this context, our group has drawn inspiration from mechanistic connections between synthetic and biocatalytic systems to explore the vast, untapped potential of nonheme enzymes for new-to-nature biocatalysis. This talk will highlight several enzymatic systems developed by our group over the past five years, which utilize diverse reaction mechanisms in transition metal catalysis for the formation of C–N, C–S, C–C, and C–halogen bonds. We hope these systems will further advance the integration of synthetic chemistry and biology to innovate chemical synthesis, as well as deepen our understanding of both biochemical and synthetic reaction mechanisms.

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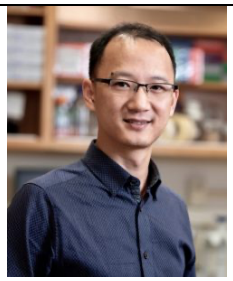

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Chemoenzymatic Strategies to Expand the Synthetic Glycome

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Complex glycans and glycoconjugates play a central role in physiological and pathological processes, generally through glycan-protein interactions. Understanding their functions and underlying mechanisms requires access to diverse, structurally well-defined glycoforms with precise linkages—a challenging task due to their inherent complexity and diversity.

The research in Li group focused on streamlining the synthesis of complex glycans and glycoconjugates and targeting the undruggable glycan-binding proteins (GBPs) for therapeutic intervention. We have developed several efficient chemoenzymatic strategies to rapidly prepare large libraries of diverse N-glycans, O-glycans, glycopeptides, and human milk oligosaccharides (HMOs). Central to these methods is the chemical synthesis of relatively simple glycan cores, followed by modular enzymatic extension to achieve structural diversity. We investigated enzyme specificities and synthetic capabilities, developing regio-selective glycosylation methods to enable efficient glycan synthesis. Over 1K well-defined molecules have been synthesized and utilized to decipher glycan-protein interactions.

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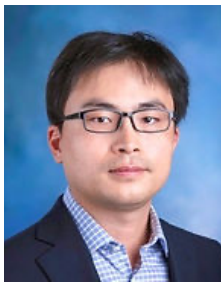

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High-Valent Copper in Catalysis

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The ability of transition metals to reach high oxidation states, particularly among second- and third-row transition metals, has enabled the development of various catalytic transformations. However, the reactivity and catalytic potential of high-valent intermediates in earth abundant metals, especially first-row late transition metals, remain poorly understood. This talk will highlight recent advances from our group in understanding the synthetic accessibility of high-valent copper complexes and their catalytic relevance. Furthermore, I will discuss our efforts to harness these elusive intermediates to develop new catalytic modes for the synthesis of biologically active molecules and their applications in biomedical imaging.

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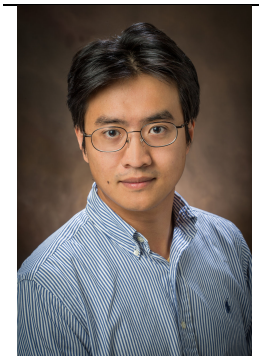

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Assembling Ternary Dead-end Complexes for Covalent Trapping of Epigenetic Modulators of Protein Methylation

Minkui Luo

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Protein lysine methylation is a distinct class of posttranslational modifications because it minimally alters the size and positive charge of lysine sidechain. In cellular contexts, the human genome encodes over ~ 60 protein lysine methyltransferases (PKMTs), ~30 lysine demethylases (KDMs), and hundreds of effector proteins to regulate thousands of lysine sites on histones and nonhistone targets in a highly orchestrated manner. The biological roles of protein lysine methylation are increasingly implicated in epigenetic regulation to define diverse cell fates, and their dysregulation is frequently associated with developmental abnormalities and various aspects of cancerous malignancy. However, it has been challenging to definitively annotate the upstream PKMTs/KDMs and the downstream effectors of known methyllysine marks. We therefore envisioned the covalent trapping (CT) technology by assembling the ternary dead-end complex of PKMTs and KDMs with substrate-cofactor surrogates. Our CT peptidic probes contain structurally distinct warheads in the place of substrate lysine paired with functionally matched cofactors or cofactor analogs. Together with the photo-crosslinking residue in proximity and the terminal biotin anchor for target enrichment, we showed that these probes are high efficient to trap epigenetic modulators of designed methyllysine marks, annotate the key players to alter disease-driven marks, and perturb them for potential epigenetic therapy.

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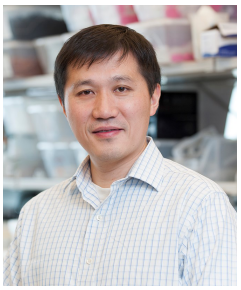

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Near-Infrared Ir(III) and Ru(II) Complexes: Photophysics and Applications for Phototherapy

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Transition-metal complexes with near-infrared (NIR) absorption and emission are desirable for a variety of applications, including telecommunication, phototherapy, bioimaging, and biosensing. Many Ir(III) and Ru(II) complexes have been reported as photosensitizers (PSs) or bioimaging reagents.[1-6] However, most of them only absorb strongly in the blue or green spectral regions. Exploration of Ir(III) and Ru(II) PSs with NIR absorption and emission has been an area of interest for photodynamic therapy (PDT), photothermal therapy (PTT), and bioimaging. We have designed and synthesized several series of mononuclear and dinuclear Ir(III) and Ru(II) complexes that exhibit strong NIR absorption and emission in the regions of 730-920 nm for PDT and/or PTT applications. Their UV-Vis-NIR absorption, emission, and fs and ns transient absorption characteristics were systematically investigated. Reactive oxygen species generation and photothermal effects for some of these complexes were studied as well. Preliminary phototherapeutic effects on 4T1 cells have been demonstrated.

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Designing Facial Amphiphilicity for Fighting Multidrug-Resistant Bacteria

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The escalating rise in antimicrobial resistance (AMR) coupled with a declining arsenal of new antibiotics is imposing serious threats to global public health. Novel therapeutics have been attempted to tackle AMR, biofilms, and persister-associated complex infections. Secondary structures of macromolecules are pivotal in the essential functions of various biological substrates, including proteins and enzymes. This macromolecular conformation is intricately linked to the spatial arrangement of functional groups and charges, which are key to achieving desired biological activities. Facial amphiphilicity is characterized by the separation of polar and nonpolar domains, a stark contrast to the linear, head-to-tail structure observed in conventional surfactants and lipids. Facial amphiphilicity plays a key role in macromolecular interactions, particularly in aqueous solutions. This property is essential in membrane proteins and peptides, influencing protein ion channels, transfection agents, and antimicrobials. The talk will focus on establishing synthetic macromolecules with facial amphiphilicity, which is highly effective to promote interactions with bacterial cell membranes. I will discuss approaches to fighting a wide variety of Gram-positive and Gram-negative bacterial strains using facially amphiphilic secondary structures to enhance interactions with bacterial membranes.

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Reactive Oxygen Species Research: Guardrails against Data Inconsistencies and Mis-Interpretations

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In all aerobic life forms, oxygen-based oxidation reactions are central to the process of powering life. Through the process of controlled "burning," formation of reactive oxygen species (ROS) is both obligatory and essential to many signaling events. However, excessive production or accumulation of ROS is harmful or even detrimental. Therefore, there is a high level of interests in studying the roles of ROS in various pathophysiological processes and in their applications in targeted delivery of drugs and imaging agents. However, the ROS research field is filled with stories of inconsistencies and lack of the ability to compare data from different publications. In this presentation, we analyze the various factors and propose the establishment of guardrails against potential pitfalls by examining issues of reaction kinetics, interfering species such as solvents and buffer components, and the need to examine individual reactive oxygen species instead of treating them collectively as a single entity.

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Cyclopropanols as Biorthogonal Warheads for Bioconjugation and Biomedical Applications

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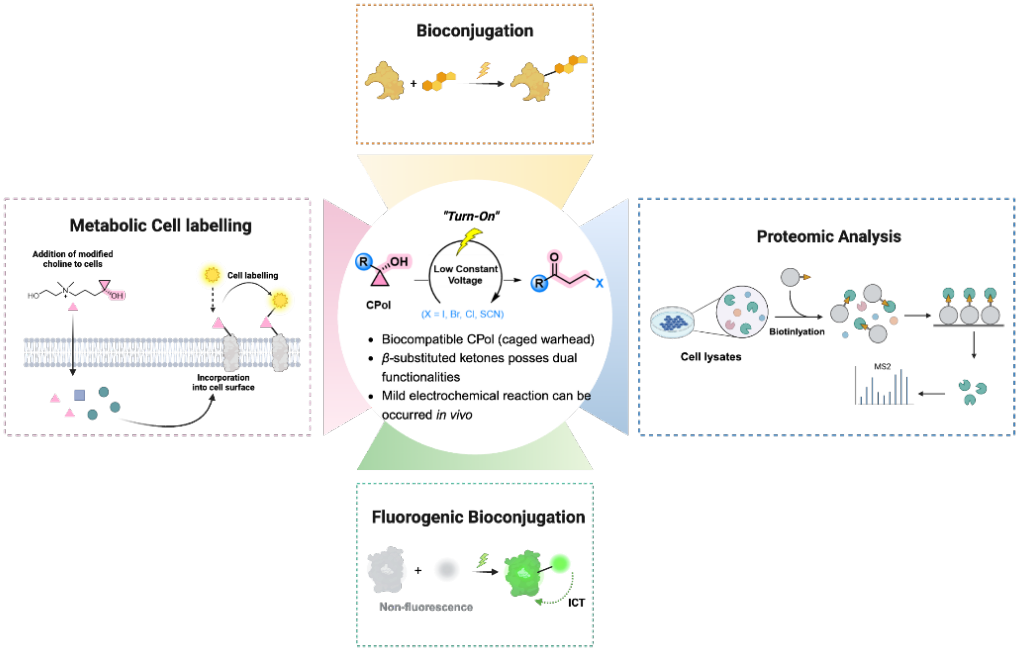
Controlling the spatial and temporal precision of bioorthogonal reactions within complex biological systems remains a significant challenge. Electrochemical activation offers a clean, mild, selective, and tunable approach for facilitating bioconjugation under physiological conditions. In this talk, I will discuss our recent development of cyclopropanol (CPol) as a bioorthogonal warhead. CPol can be selectively activated through electrochemical or chemical stimuli under physiological conditions, generating ketone moieties with dual functionality. These moieties enable diverse applications, including protein conjugation, new covalent inhibitor, cell surface labeling, and proteomic analysis. Our findings establish CPol and related compounds as "caged" warheads, serving as highly versatile functional groups for advanced bioconjugation strategies.



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Physics-Guided Protein Engineering

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My group seeks to redefine protein engineering by anchoring it in molecular-level physical principles. We are developing Mutexa, a physics-informed artificial intelligence (AI) platform for "intelligent" protein engineering, enabling researchers to identify super-mutants with non-native functional performance while uncovering the molecular insights behind unpredictable experimental outcomes. Protein engineering, despite over decades of progress, remains reliant on labor- and resource-intensive experimental screening, which delivers only "what you screen for" and offers little insight into the structure-function relationships underlying mutation effects. While AI is widely recognized for its potential to accelerate protein engineering, I question the feasibility of achieving generalizable predictive models through AI alone.

In this talk, I will present the technical foundations of Mutexa and its application in two protein engineering challenges: one for designing industrial bidomain enzymes that maintain high activity at lower temperatures (known as cold-adapted enzymes), and the other for predicting the structures of lasso peptides, a class of ribosomally synthesized and post-translationally modified peptides, as antibiotics. These applications showcase Mutexa's unique ability to drive the discovery of functional proteins beyond traditional screening-based approaches, offering solutions for sustainable biomanufacturing and antimicrobial development.

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Advancing Drug Discovery by Targeting Protein Tyrosine Phosphatases

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Aberrant cellular signaling stemming from altered protein tyrosine phosphorylation is a major contributing factor to human diseases including cancer, diabetes, neurodegenerative and autoimmune disorders. Consequently, anomalous cellular events driven by defective protein tyrosine phosphorylation afford tremendous opportunities for targeted intervention. Success for such targeted approach is evident by the abundance of kinase-based therapeutics that have become important treatment modalities. Given the reversible nature of protein tyrosine phosphorylation, there is great potential to manipulate disease biology at the level of protein tyrosine phosphatases (PTPs). However, despite increasing interest in the PTPs, they still remain largely an underexploited target class. Among major factors that contribute to the difficulty of PTP-based drug discovery are incomplete understanding of how PTP malfunction causes diseases and insufficient target validation. In addition, there is the general lack of PTP-specific small molecule probes for functional interrogation, target validation, and therapeutic development. In this presentation, I describe our recent work on oncogenic PTPs that yield new insights into their roles in tumorigenesis. Improved knowledge of the PTP-mediated disease mechanisms is essential for designing new therapeutic strategies. I also discuss several approaches for the acquisition of highly potent and selective PTP inhibitors with efficacious *in vivo* activity. Potent and specific PTP inhibitors facilitate functional analysis of the PTPs in complex signal transduction pathways and may constitute novel therapeutics for a wide range of human diseases.

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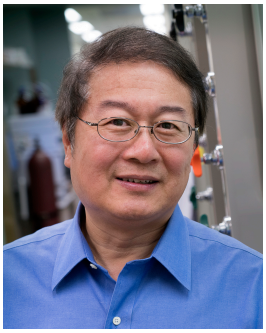

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