

RNA Recognition and Targeted Degradation: Mechanisms and Engineering Strategies based on RNA-Binding Domains (RBDs)



Invited Speaker

Fan Yang

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Date: August 20, 2025 (Wednesday)

Time: 15:00-16:00 (Hong Kong Time)

Location: 5405, Li Building, CityU

Biography

Fan Yang is Professor at the School of Life Science and Technology, Harbin Institute of Technology, and head of the Biomolecular NMR Laboratory. She received her B.S. from Peking University and conducted postdoctoral research at the University of Washington. Her work focuses on RNA-protein interactions, mechanisms of RNA regulation, and the design of proteins and peptides targeting disease-related RNAs.

Abstract

RNA-binding proteins (RBPs) control RNA fate by recognizing specific motifs and structures, yet how they achieve high selectivity and can be repurposed for intervention remains unclear. Using RbFox as a model, we combined HiTS-Eq and solution NMR to uncover two binding modes: one with high affinity for cognate RNAs and another accommodating non-cognate substrates with lower affinity. Structural analyses revealed RNA-dependent conformational changes extending beyond the binding site, indicating that RNA can function as an allosteric effector. Exploiting these insights, we engineered RbFox RNA recognition motifs to target stem-loop RNAs, including miRNA precursors, thereby modulating processing and reducing cancer cell viability. In parallel, we designed artificial RNA-cleaving RBPs by introducing electrostatic catalytic features. Guided by modeling and NMR, these constructs integrate recognition and catalysis in a compact, programmable format, offering guide-free alternatives to CRISPR-based systems with the ability to target structured RNAs. Together, our work uncovers principles of RNA-protein selectivity and allosteric regulation, while establishing versatile strategies for RNA targeting and manipulation with therapeutic potential.