Rice University
George R. Brown School of Engineering
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Presents

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Herzstein Hall 210

Discovery, Engineering, and Therapeutic Applications of Small Molecules and Macromolecules from Microbes

Nature's ability to generate diverse molecular structures enables microbes to produce powerful biomolecules as valuable therapeutics. Small bioactive molecules from microbes play an essential role in modulating the biological activities of targets implicated in diseases and serve as leads for therapeutic development. Additionally, the recently discovered microbial ribonucleoprotein, CRISPR/Cas9, in complex with a single guide RNA, has been extensively applied to mediate genome editing both in vitro and in vivo as next-generation therapeutics. With the recent advances in the DNA sequencing technologies, microbial genomes and metagenomes from various microbial communities are serving as treasure troves, encoding numerous unelucidated genetic information. Novel small molecules and macromolecules needed to meet the demand for new treatments of diseases remain largely unexplored. In this talk, I will first present deep mechanistic investigations of the enzymatic machinery for the biosynthesis of structurally complex natural products. By understanding the enzymatic basis of these complex architectures, I identified and engineered a key biosynthetic enzyme to be the ideal biocatalyst for manufacturing the cholesterol-lowing drug Simvastatin. In the second part of my presentation, I will describe the design and development of in vivo delivery of Cas9: guide RNA complex in an animal model of human genetic hearing loss disease. Exploiting the superb specificity of the Cas9:guide RNA protein delivery system, we applied a permanent modification of genomic DNA with incredibly low off-target activity and observed the avoidance of hearing loss in mice. Our results suggest a strategy of direct protein:RNA delivery for genome-editing in somatic cells in vivo as a potential treatment for certain genetic hearing loss diseases.

About the Speaker

Dr. Xue Gao is a postdoctoral associate in the Department of Chemistry and Chemical Biology at Harvard University. She is currently working in the laboratory of Professor David R. Liu, where she is developing treatment of genetic hearing diseases by in vivo delivery of CRISPR/Cas9 genome editing agents. Dr. Gao obtained her doctoral degree in Chemical and Biomolecular Engineering from University of California, Los Angeles in 2013. She was the only graduate student recipient of the 2013 Harry M. Showman Prize across all fields in the School of Engineering at UCLA. Her graduate research in Professor Yi Tang's laboratory focused on the investigation of enzymatic mechanisms of fungal natural products biosynthesis and further engineering of enzymes as powerful catalysts for manufacturing important pharmaceuticals. Her work with Professor Tang and industrial collaborator Codexis® on the development of an efficient biocatalytic process to manufacture simvastatin won the 2012 Presidential Green Chemistry Challenge Award. Dr. Gao received both of her Bachelor's and Master's degrees in Chemical Engineering at Tianjin University with the guidance of Prof. Yingjin Yuan. Her future research interests include utilizing synthetic biology approaches to identify and engineer powerful biomolecules from microbial sources for therapeutics.