

UC San Diego

JACOBS SCHOOL OF ENGINEERING  
Aiiiso Yufeng Li Family Department of  
Chemical and Nano Engineering

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## DEPARTMENT SEMINAR

Wednesday, November 6th, 2024

11:00 AM - 12:00 PM

SME 248



Dr. Yuzhong Liu, PhD

*“Microbial hosts as a biosynthetic platform to  
make complex (un)natural glycosides”*

Assistant Professor

Department of Chemistry

Scripps Research

**Abstract:** QS-21 is a potent vaccine adjuvant and remains the only saponin-based adjuvant that has been clinically approved for use in humans. However, owing to the complex structure of QS-21, its availability is limited. Today, the supply depends on laborious extraction from the Chilean soapbark tree or on low-yielding total chemical synthesis. Here we demonstrate the complete biosynthesis of QS-21 and its precursors, as well as structural derivatives, in engineered yeast strains. The successful biosynthesis in yeast requires fine-tuning of the host’s native pathway fluxes, as well as the functional and balanced expression of 38 heterologous enzymes. The required biosynthetic pathway spans seven enzyme families—a terpene synthase, P450s, nucleotide sugar synthases, glycosyltransferases, a coenzyme A ligase, acyl transferases and polyketide synthases—from six organisms, and mimics in yeast the subcellular compartmentalization of plants from the endoplasmic reticulum membrane to the cytosol. Finally, by taking advantage of the promiscuity of certain pathway enzymes, we produced structural analogues of QS-21 using this biosynthetic platform. This microbial production scheme will allow for the future establishment of a structure-activity relationship, and will thus enable the rational design of potent vaccine adjuvants.

**Bio:** Dr. Yuzhong Liu obtained her PhD in Chemistry from University of California, Berkeley studying dynamic porous materials for carbon capture. In 2018, she started her postdoctoral research at the Joint Bio-Energy Institute (JBEI) and Lawrence Berkeley National Laboratory focusing on the sustainable production of complex natural products through heterologous pathway expression in microbial hosts. In particular, she achieved the complete biosynthesis of QS-21 in engineered yeast, which remains the only saponin-based vaccine adjuvant approved by the FDA. In the meantime, Yuzhong also served as the Associate Director of Commercialization at JBEI, as well as a scientific consultant for Bay Area Biotechnology startups to help transition technology from the research lab towards real-world applications. Yuzhong started her independent career at Scripps Research (the other Scripps) in August 2023 and her lab focuses on the biosynthesis of complex natural and unnatural glycosides to advance vaccine development.

Seminar Host: Yanran Li