Chemical Engineering

Spring 2024 Seminar Series

Predicting and Engineering Cellular Functions for Ultra-Safe Living Technologies

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4:00pm Reception

Engineered cells can address unmet needs for human and planetary health, including the controlled production of drugs or degradation of hazards in situ. To develop safe cell-based technologies, we need cellular engineering tools that 1) predict and design phenotypes and 2) control proliferation.

In the first part of my talk, I will discuss my work targeting malaria parasites through the understanding of cellular metabolism. I developed mathematical formulations that identify cellular processes underlying phenotypes, nutritional requirements, and high-order synthetic lethal interactions. I constructed the most comprehensive genome-scale metabolic models of highly uncharacterized malaria parasites and achieved 80% accuracy in essentiality predictions, as proven by experimental data. In this collaborative project with experts in malaria, I co-discovered seven metabolic pathways essential for survival in liver-stage malaria parasites. This knowledge is guiding the design of metabolically attenuated parasites for a malaria vaccine.

In the second part of my talk, I will present my project on engineering an ultra-safe strain of Escherichia coli. Currently, bacteria used as platform technologies rely on a wild-type genetic code, which can result in horizontal gene transfer, escape, and loss of control of the designed programs. Genetic code engineering emerges as a promising alternative since it removes a set of codons and tRNAs from the genome. Without the possibility to read all wild-type codons, bacteria with an engineered genetic code should not translate incoming DNA. Fascinatingly, I discovered a new mechanism of escape in bacteria with an engineered genetic code and characterized it with multi-omics and protein language models. This finding allowed me to develop an ultra-safe 61-codon E. coli strain. In this strain, I engineered a tRNA/aminoacyl-tRNA synthetase pair for the incorporation of a non-standard amino acid and implemented kill switches. This is the first organism that enables the production of proteins containing user-defined non-standard amino acids while remaining tightly biocontained and bioisolated.

My work is a head-start to develop ultra-safe living technologies and will allow us to decode and expand genome and protein designs.

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