SYNTHETIC BIOLOGY PLATFORMS FOR NATURAL PRODUCT BIOSYNTHESIS AND DISCOVERY

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Plants are a rich source of unique scaffolds, including 25% of natural-product-derived drugs. However, the discovery, synthesis, and overall material supply chains for sourcing plant natural products and their derivatives remain ad hoc, biased, and tedious. While microbial biosynthesis presents compelling alternatives to traditional approaches based on extraction from natural plant hosts, many challenges exist in the reconstruction of plant specialized metabolic pathways in microbial hosts. My laboratory has developed approaches to address the challenges that arise in the reconstruction of complex biosynthesis schemes, including spatial engineering strategies to direct the activities and specificities of pathway enzymes and recoding strategies to address folding, processing, and stability issues that may arise with the expression of plant enzymes in heterologous microbial hosts. We have utilized these strategies to develop yeast-based production platforms for an important class of plant alkaloids, the benzylisoquinoline alkaloids, including the medicinal opioids. These synthetic biology platforms will lead to transformative advances in natural product discovery, drug development, and production.