Evolutionary Optimization of Heterologous Metabolic Pathways in Microbes

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Reception: 3:30 p.m. - Benson Lobby

Abstract

Our ability to engineer microbial metabolic pathways is improving rapidly, enabling the efficient and sustainable biosyntheses of both bulk and fine chemicals. However, novel pathways frequently require significant optimization to function efficiently in a new production host. More precisely, optimization is a complex co-adaptation process, as the host must accommodate its new pathway and the pathway adjust to its new host. The interactions between pathway and host, as well as their evolutionary outcomes, will determine whether natural and engineered microbes can produce biochemicals, remediate polluted sites, or become pathogenic.

I will demonstrate how a combination of rational and evolutionary approaches targeted to both an enzyme and its host can be used to increase the activity of a heterologous monooxygenase by more than 50-fold. Next, I will discuss the need for evolutionary refinement of horizontally-transferred genes, using dichloromethane catabolism in *Methylobacterium extorquens* as a model system. By contrasting these two examples, I will show how engineering tools can provide new insight into natural evolutionary processes and how evolutionary microbiology can provide new strategies for forward engineering. Finally, I will discuss future directions in this area, with applications ranging from bioremediation to the production of renewable biochemicals.

Speaker Biography

Joshua Michener is an NRSA Postdoctoral Fellow in the Biological Engineering Department at MIT, where he studies microbial evolution after horizontal gene transfer. He received his PhD in Bioengineering with Christina Smolke at Caltech, for research on yeast metabolic engineering, and an SB in Chemical Engineering from MIT. His research seeks to understand how microbes respond after acquiring new genetic material, either through synthetic biology or horizontal gene transfer.