Metabolic engineering holds great promise for creating efficient, competitive routes for the production of biofuels and biochemicals without the necessity for harsh chemicals and hazardous byproducts. Successes in biochemical production include the production of DuPont's Sorona fibers from 1,3-propanediol from glucose using bacteria and the manufacture of the anti-malarial drug artemisinin from yeast. However, roadblocks to biosynthesis prevent many biochemicals from being produced biologically given current technology. Nature uses compartmentalization (e.g. in organelles in eukaryotes and in bacterial microcompartments in prokaryotes) to solve issues such as intermediate leakage, toxicity, and byproduct formation. Here we propose to deploy compartmentalization as a strategy to overcome a critical roadblock: the requirement for redox cofactor recycling. In traditional systems, redox cofactors are lost to cellular growth and maintenance needs. By compartmentalizing redox cofactors with the biochemical synthesis enzymes, we anticipate increasing the thermodynamic efficiency and preventing the loss of valuable intermediates and cofactors. If successful, it would be the first direct demonstration of this feature of a bacterial microcompartment, and would provide a tool for improving metabolic pathway performance for all enzymes with redox or other cofactors. Our specific objectives are to engineer a private NADH pool for 1,3-propanediol and fatty acid biosynthesis and use kinetic metabolic models to inform the design and optimization of these systems.

We will couple modeling with experiments and uncover the best way to improve each engineered metabolic pathway’s performance. If successful, this work would provide insight into the native function of these structures, while also providing a detailed method for selecting and improving biochemical pathway performance. Ultimately, this will lead to the cost-efficient production of chemicals that are currently derived from petroleum.

The research team will be lead by Dr. Danielle Tullman-Ercek who will collaborate with Dr. Keith Tyo and Dr. Niall Mangan all at Northwestern University.

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