

ENGINEERED POLYKETIDE SYNTHASES FOR PRODUCTION OF COMMODITY AND SPECIALTY CHEMICALS

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Engineered modular polyketide synthases (PKSs) have the potential to be an extraordinarily effective retrosynthesis platform. Native PKSs assemble and tailor simple, readily available cellular acyl-CoAs into large, complex, chiral molecules. By successfully rearranging existing polyketide modules and domains, one can exquisitely control chemical structure from DNA sequence alone. As an example of the diverse biosynthetic potential of PKSs, we have concluded that approximately 20 of the roughly 150 commodity chemicals tracked by the petrochemical market information provider ICIS could be produced by mixing and matching naturally occurring PKS domains. To form these chemicals, engineered PKSs load acyl-CoAs, perform a programmed number of extension reactions, and then release products using previously published mechanisms. However, this potential has only just begun to be realized as the compounds that have been made using engineered PKSs represent a small fraction of the potentially accessible chemical space. In my talk, I will highlight work from our laboratory in which we have engineered polyketide synthases to produce a variety of commodity and specialty chemicals and expressed these engineered PKSs in a variety of *Streptomyces* for production of these molecules from sugars and other inexpensive starting materials.