Title: The development of an automated platform for the use of Polyketide Synthases for Biofuels and Sustainable Chemical Production

Alberto Nava[4] (aanava@lbl.gov), Robert Haushalter[1,3], Tyler Backman[1,3], Cameron Coates[1,2], Nurgul Kaplan Lease[1,2], Zilong Wang[1,3], Ramu Kakumanu[1,3], Bashar Amer, Edward Baidoo, **Jay D. Keasling[1,3,4]**

[1]DOE Joint BioEnergy Institute; Emeryville, CA 94608, USA; [2]DOE Agile BioFoundry; Emeryville, CA 94608, USA; [3]Lawrence Berkeley National Laboratory; Berkeley, CA 94720, USA, [4]University of California, Berkeley, 94720 CA, USA.

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Project Goals:
This projects aims to establish an automated platform for the rational design and engineering of PKSs to produce biofuels and biochemicals. The application of retrobiosynthesis and data-driven, high-throughput workflow are being combined to identify targets and engineer PKS pathways for their production.

Abstract text.
Retrobiosynthesis is an approach to the design of biosynthetic pathways, which involves simulating possible biosynthesis routes in reverse, one step at a time. Modular type I polyketide synthases (PKSs), due to their collinear biosynthetic logic, have enormous potential as a retrobiosynthesis platform and have recently been engineered to produce several biofuels and bioproducts. However, the full potential of PKSs has yet to be realized for a variety of reasons including difficult cloning and heterologous expression due to the prevalence of repetitive sequences, their large size, as well as an incomplete understanding of protein-protein and substrate-protein interactions. With rapid advances in the fields of automation, machine learning, DNA synthesis, and DNA sequencing, a data-driven approach to exploring and optimizing PKS function becomes an attractive method. Here we present our work at the Joint Bioenergy Institute (JBEI) to develop an automated platform for the rational design and engineering of PKSs. We present preliminary results on the efficacy and throughput of the platform as well as preliminary characterization studies of novel chimeric PKSs. Work is ongoing to integrate features of the PKSs and their observed behavior into a model which may be used for the prediction of optimal chimeric PKSs

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