(SD2018-178) Engineering Polyketide Synthase Machinery in Synechococcus Cyanobacteria

Tech ID: 29938 / UC Case 2018-178-0

BACKGROUND

Complex polyketides include a family of natural products that possess a wide variety of pharmacological or biological activities. Numerous polyketides and their semisynthetic derivatives have been approved for clinical use in humans or animals, including antibiotics, antifungal agents, immunosuppressants, antiparasitic agents and insecticides. All these natural products share a common mechanism of biosynthesis and are produced by a class of enzymes called polyketide synthases (PKSs). Besides their essential role in the biosynthesis of a vast diversity of natural products, the versatility of PKSs can be further emphasized as they can be redesigned and repurposed to produce novel molecules that could be used as fuels, industrial chemicals, and monomers. Most polyketide producers are slow-growing, recalcitrant to genetic manipulation, or even non-culturable.

Cyanobacteria are particularly attractive for the production of natural compounds because they have minimal nutritional demands and several strains have well established genetic tools.

TECHNOLOGY DESCRIPTION

Researchers from UC San Diego and Rosario National University (Argentina) have invented a novel functional heterologous PKS system expressed in a photosynthetic microorganism (cyanobacterium: *Synechococcus*). This patented technology, allows for the production of precursors and the expression of accessory proteins, and serves as a platform for production of a wide variety of polyketide products. These includes small molecules useful as medicinal natural products, biofuels, and polymer precursors.

The development of a photosynthetic PKS producing host will prove valuable for low cost, high volume production of valuable small molecules, and we are currently evaluating culture scale-up on the +100 liter level as proof of concept.

On the basis of this platform technology, other methylmalonyl-CoA derived polyketides could be produced in a sustainable and profitable manner by changing the third module with the desired PKS. Further, other PKS classes that require malonyl-CoA, ethylmalonyl-CoA, and other CoA precursors should be accessible by this approach. For additional details, please refer to the cited publication.

APPLICATIONS

This work is a foundational step forward for the production of high value polyketides in a photosynthetic microorganism.

ADVANTAGES

This invention is the first time that a functional heterologous PKS system has been expressed in a photosynthetic microorganism, *S. elongatus*

It is noteworthy that S. elongatus does not have its own PKS genes, thus acting as a biosynthetically naïve host which offers superior genetic manipulation capabilities making it a clean host for polyketide production.

The development of a photosynthetic PKS producing host will prove valuable for low cost, high volume production of valuable small molecules.

STATE OF DEVELOPMENT

The inventors are currently evaluating culture scale-up on the +100 liter level as proof of concept.

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OTHER INFORMATION

KEYWORDS

heterologous production, Cyanobacteria, polyketide, PKS-derived compounds, synthetic biology, photosynthetic organism, Metabolic Engineering, Genetically-Modified, Synechococcus

CATEGORIZED AS

- **Agriculture & Animal Science**
  - Transgenics
- **Biotechnology**
  - Industrial/ Energy

RELATED CASES

2018-178-0

INTELLECTUAL PROPERTY INFO

UC San Diego is offering US patent rights for commercialization. It is available for licensing.

(12) **United States Patent**
Burkart et al.

(10) **Patent No.: US 11,274,324 B2**
(45) **Date of Patent: Mar. 15, 2022**

(54) **ENGINEERING POLYKETIDE SYNTHASE IN CYANOBACTERIA**

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RELATED MATERIALS

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PATENT STATUS

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