Docket #: S15-017

Gene sequences for the biosynthesis of podophyllotoxin derivatives

Stanford researchers at the Sattely Lab have discovered six podophyllotoxin biosynthetic genes and their polypeptide products from the plant, Podophyllum hexandrum (mayapple). This discovery enables the engineering of alternative biological hosts for the production of a direct precursor for the semi-synthesis of Etopophos, an FDA approved anticancer agent. The genes and their polypeptide products were elucidated by RNA-Seq analysis and their activities were demonstrated by in vivo and in vitro testing.

Figure

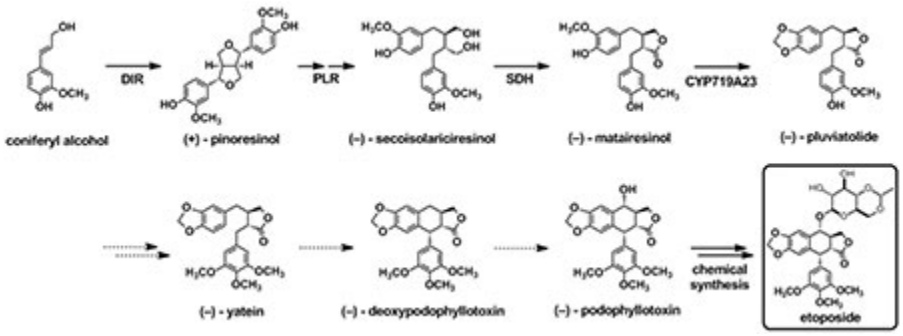

Figure description - Biosynthetic pathway of (–)-podophyllotoxin in *P. hexandrum*

Stage of Research

- Proof-of-concept
- Used bioinformatics, heterologous enzyme expression, and kinetic characterization, to work out the pathway that makes the precursor in mayapple then successfully transplanted the full biosynthetic pathway into tobacco plants
- Other genes yet be further explored

Applications

- Biosynthesis of a podophyllotoxin derivative as a precursor to the FDA approved anticancer agent, Etopophos, in engineered biological hosts

Advantages

- Enables a **preferred, biosynthetic method** for producing podophyllotoxin by engineering a microbial host for industrial fermentation
- **Less costly and more direct production route** to Etopophos
- **Relieves severe pressure on endangered natural sources.** Podophyllum hexandrum, a slow-growing plant, is regarded as an endangered species

Publications

- Lau, W. and Sattely, E. S. "Six genes that complete biosynthetic pathway to the etoposide aglycone in Mayapple" Science, 2015, 349, 1224-1228.

Patents

- Published Application: 20170088872

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