

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

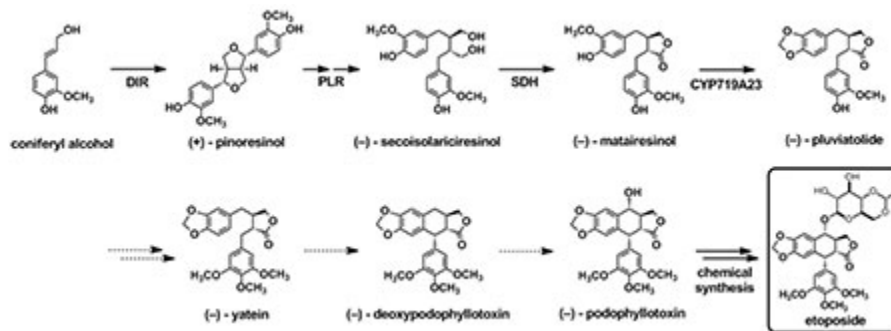


Figure description - Biosynthetic pathway of (-)-podophyllotoxin in *P. hexandrum*

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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