Bioengineering triacetic acid lactone production in Yarrowia lipolytica for pogostone synthesis

Yarrowia lipolytica is an oleaginous yeast that is recognized for its ability to accumulate high levels of lipids, which can serve as precursors to biobased fuels and chemicals. Polyketides, such as triacetic acid lactone (TAL), can also serve as a precursor for diverse commodity chemicals. This study used Y. lipolytica as a host organism for the production of TAL via expression of the 2-pyrene synthase gene from Gerbera hybrida. Induction of lipid biosynthesis by nitrogen-limited growth conditions increased TAL titers. We also manipulated basal levels of TAL production using a DNA cut-and-paste transposon to mobilize and integrate multiple copies of the 2-pyrene synthase gene. Strain modifications and batch fermentation in nitrogen-limited medium yielded TAL titers of 2.6 g/L. Furthermore, we show that minimal medium allows TAL to be readily concentrated at >94% purity and converted at 96% yield to pogostone, a valuable antibiotic. Modifications of this reaction scheme yielded diverse related compounds. Thus, oleaginous organisms have the potential to be flexible microbial biofactories capable of economical synthesis of platform chemicals and the generation of industrially relevant molecules.

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