

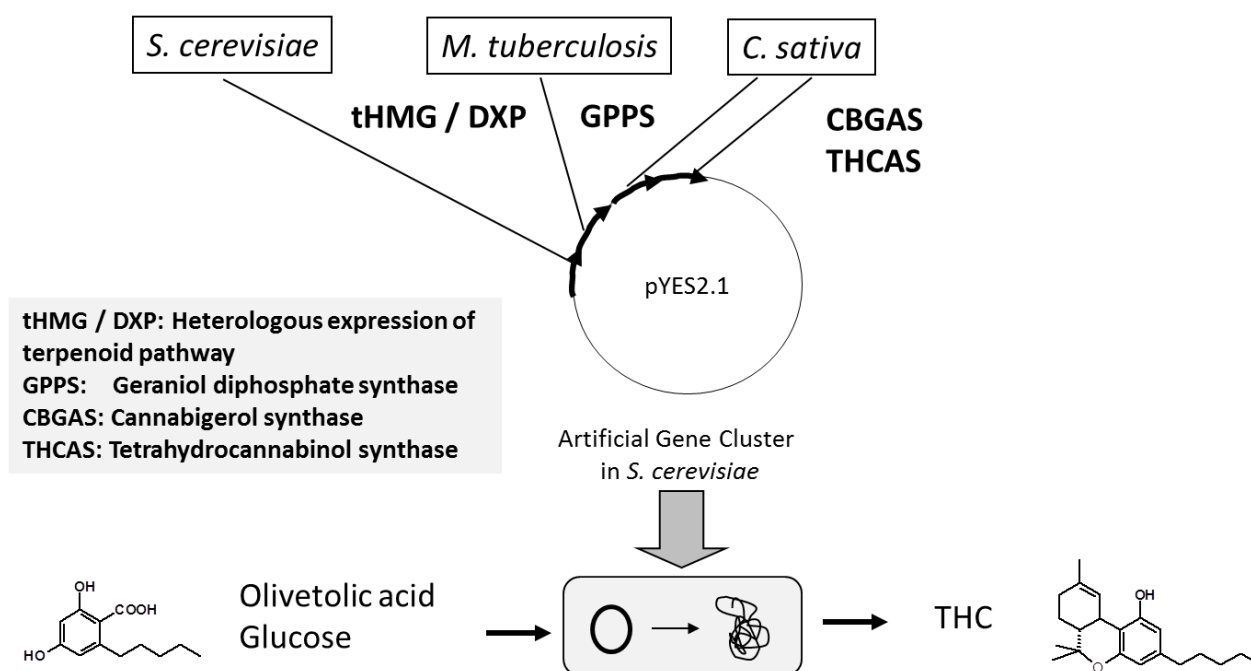
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## BIOENGINEERING AND BIOCATALYST DESIGN FOR THE PRODUCTION OF RECOMBINANT DELTA-9-TETRAHYDROCANNABINOLIC ACID (THCA)

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Delta-9-Tetrahydrocannabinolic acid (THCA) is an important drug from *Cannabis sativa* L. with psychomimetic activities. THCA and related herbal products are mostly misused and illegal use is dominated despite the fact that THCA has a significant medicinal value. Today, breeding and cultivation of high content plants is not legal for extraction, but also organic synthesis is too expensive and not efficient to obtain high amount of THCA and its corresponding decarboxylated THC derivative for industrial production. Biotechnology may provide new avenues for biosynthesis and production strategies, but the biosynthesis *in planta* is not fully elucidated, why heterologous expression of biosynthetic genes is complicated. Herein we provide an overview of recent developments on the elucidation of the pathway towards cannabinoids and updated attempts for construction of a recombinant host for the production of THCA and its main precursors CBGA and GPP. In short plants genetics, transcriptomics and metabolomics of trichomes where biosynthesis is localized will be discussed, principles of gene expression of the main important genes (CBGA-Synthase, THCA-Synthase) will be explained, and into basic concepts of bioengineering of yeasts as potential hosts will be introduced.



[1] Happyana, N. et al. (2013) Analysis of cannabinoids in laser microdissected trichomes of medicinal *Cannabis sativa* using LCMS and cryogenic NMR. *Phytochemistry* 87:51-59.

[2] Muntendam, R et al. (2009) Perspectives and limits of engineering the isoprenoid metabolism in heterologous hosts *Appl. Microbiol Biotechnol.* 84:1003-1019.