BIOTRANS
LA ROCHELLE 2023

N°156 / OC
TOPIC(s) : Biocatalytic cascade reactions / Synthetic biology, metabolic engineering

Terpene factory

AUTHORS
Létitia LEYDET / AIX-MARSEILLE UNIVERSITE, CAMPUS ETOILE, ENSEMBLE TPR,52 AV. ESCADRILLE NORMANDIE NIÉMEN, MARSEILLE
Gilles IACAZIO / AIX-MARSEILLE UNIVERSITE, CAMPUS ETOILE, ENSEMBLE TPR,52 AV. ESCADRILLE NORMANDIE NIÉMEN, MARSEILLE
Katia DUQUESNE / AIX-MARSEILLE UNIVERSITE, CAMPUS ETOILE, ENSEMBLE TPR,52 AV. ESCADRILLE NORMANDIE NIÉMEN, MARSEILLE
Agnès AMOURIC / AIX-MARSEILLE UNIVERSITE, CAMPUS ETOILE, ENSEMBLE TPR,52 AV. ESCADRILLE NORMANDIE NIÉMEN, MARSEILLE

PURPOSE OF THE ABSTRACT
Terpenoid are one of the most represented families of natural molecules on Earth. To date, more than 100,000 compounds [1] whose structural, biological (antibiotic, anticancer, anti-inflammatory, etc.) and physicochemical (cleaner, flavor, dye, etc.) properties hold the attention of the scientific community [2-3]. However, their access is limited because of the low available quantity by extraction from natural sources ; an often expensive and laborious chemical synthesis ; and long biosynthetic pathways. We have developed a new in vitro production pathway[4] : two enzymes making it possible to obtain diphosphates (DMAPP and IPP the universal precursors of terpenes), a prenyl transferase and finally the enzyme allowing cyclization. This synthesis is carried out from two alcohols with five carbon atoms in order to give different terpene compounds.
In our case, one terpene from each family is selected: santalene, squalene, taxadiene and lycopene (respectively for sesquiterpene, triterpene, diterpene and teraterpene synthases).
By combining bioinformatics, biochemical and molecular biology approaches, we have developed this approach in vivo, by joining together two plasmids comprising the two genes necessary for this mini-pathway. Playing on the gene position, but also on the different regulatory elements(operonic organization, RBS shuffling,...), the quantity of terpenes obtained can vary : it is a question of optimising the experimental conditions, from genetic construction to bioconversion.
In the future the objective is to apply theses approaches to all terpenoids and that it may represent a new biosynthetic tool of interest to optimize and facilitate access to current terpenes, but also to explore biodiversity and characterize new terpene synthases.

FIGURES

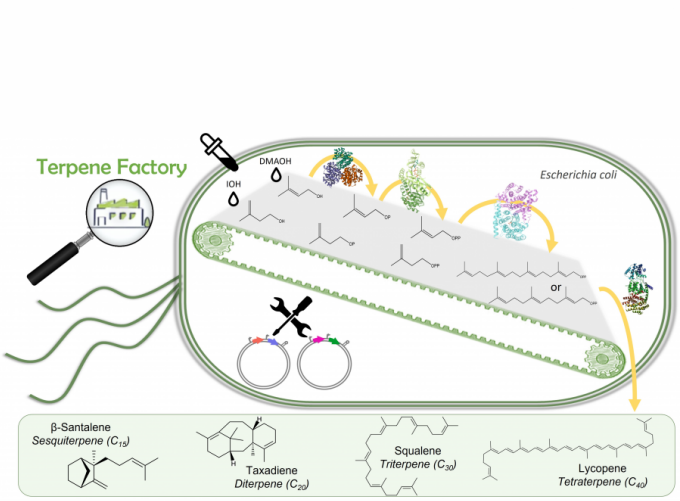

FIGURE 1

Terpene factory

Genetically modified bacteria capable of producing terpenes through associated enzymes.

FIGURE 2

KEYWORDS

Biocatalysis | Terpene | Synthetic biology | In vivo

BIBLIOGRAPHY

[1] Xiaoqiang Ma, Hong Liang, Qiuchi Pan, Kristala L. J. Prather, Anthony J. Sinskey, Gregory Stephanopoulos, and Kang Zhou, Optimization of the Isopentenol Utilization Pathway for Isoprenoid Synthesis in Escherichia coli, J. Agric. Food Chem. 2022, 70, 3512-3520

[2] Bohlmann J, Keeling CI. Terpenoid biomaterials. Plant J. (2008) 54(4):656-69.

[3] Paramasivan K, Mutturi S. Progress in Terpene Synthesis Strategies through Engineering of Saccharomyces cerevisiae. Crit. Rev. Biotechnol. (2017) 37(8):974-989.

[4] Couillaud J, Rico J, Rubini A, Hamrouni T, Courvoisier-Dezord E, Petit JL, Mariage A, Darii E, Duquesne K, de Berardinis V, Iacazio G. Simplified in Vitro and in Vivo Bioaccess to Prenylated Compounds. ACS Omega. (2019) 4(4), 7838-7849.