הטכניון - מכון טכנולוגי לישראל

TECHNION - ISRAEL INSTITUTE OF TECHNOLOGY

הפקולטה להנדסה כימית
ע"ש וולפסון
The Wolfson Department of Chemical Engineering

Wolfson Department of Chemical Engineering Seminar

Wednesday, March 12th, 2025 at 12:30 (Israel time)/18:30 (Beijing time)

ZOOM Link:
https://gtiit.zoom.us/j/94583771409?pwd=1Hb7qSSYtldJ6z1IP1wqCqELMtxowX.1

Metabolic Engineering of *Yarrowia lipolytica* for Biosynthesis of Punicic Acid via Acetate-Glucose Co-Substrate

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MSc Seminar

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Abstract

Punicic acid (PuA) is a conjugated linolenic acid (CLA) that naturally presented in the arils of pomegranate with anti-inflammatory, cardio-protective and anti-cancer effect. Current CLA production by fermentation heavily relies on glucose-based media, bringing problems on efficiency and sustainability.

This seminar presents our effort to improve PuA production by combining metabolic engineering with process optimisation in *Yarrowia lipolytica* acetate-glucose co-substrate fermentation. *Y. lipolytica* are genetically modified with Cre-loxP technique for multiple gene integrations and deletions. Overexpression of key genes for acetate utilisation provides *Y. lipolytica* with abundant acetyl-CoA for fatty acid synthesis and energy supply, accompanying a high tolerance to acetate. Deletion of competing pathway further improves fatty acid yield. Increasing the copy number of a key gene encoding fatty acid conjugase from pomegranate plant overcomes the main bottleneck. Next, engineered strains are tested in acetate-glucose co-substrate fermentation with various acetate concentration after adaptation, where the effect of fermentation temperature and feeding strategy are investigated to further alleviate acetate toxicity and increase production.

Co-feeding of acetate with glucose in fermentation media alters the fatty acids profile, leading to a shift of monounsaturated fatty acid toward polyunsaturated fatty acid synthesis (C18:2), which accounts for more than 60% of the total fatty acids. The final engineered strain accumulated about 3.8% of PuA. This demonstrates the potential to harness yeast metabolism to produce high-value conjugated unsaturated fatty acid from renewable and low-cost carbon sources.