Moorella thermoacetica: a chassis organism for biochemicals production?

Barbara Bourgade\textsuperscript{1}, Brahim Benyahia\textsuperscript{1}, Nigel Minton\textsuperscript{2}, M. Ahsanul Islam\textsuperscript{1}

\textsuperscript{1}Department of Chemical Engineering, Loughborough University
\textsuperscript{2}Synthetic Biology Research Centre, University of Nottingham

Introduction

Microbial chassis organisms are crucial for chemicals bioproduction. Indeed, modern genetic tools allow to modify or insert genes in these organisms to synthesise desired target compounds. Acetogenic bacteria, or acetogens, are promising hosts as they convert CO and CO\textsubscript{2} into acetate and other products during gas fermentation.

The acetogen Moorella thermoacetica is interesting for industrial gas fermentation as its thermophilic requirements limit cooling processes. Thus, this project focuses on creating synthetic pathways and implementing them in M. thermoacetica to produce platform chemicals.

Pathway design

To produce non-native compounds, synthetic metabolic pathways have been designed using the computational tools From Metabolite to Metabolite\textsuperscript{1} and Metabolic Route Explorer\textsuperscript{2}. The chosen targets are widespread industrial chemicals, such as ethylene glycol or 1,2-propanediol. After pathway design, different pruning criteria, including gene availability or pathway length, are applied to select the best candidate pathways.

CREATING SYNTHETIC PATHWAYS

- Pathway Design
  - From Metabolite to Metabolite
  - Metabolic Route Explorer

- Pathway Analysis
  - Genome-scale and constraint-based analysis
  - Flux Balance Analysis
  - Thermodynamics analysis

Further genome-scale analysis excludes inappropriate pathways. For example, the constraint-based COBRA\textsuperscript{3} toolbox is used to assess pathway feasibility in the genome-scale model of M. thermoacetica.

Pathway Implementation

Once feasible pathways have been selected, implementation in M. thermoacetica is attempted to produce the chosen target compounds. However, this first requires to improve and develop genetic tools for this organism. Indeed, although some tools have been created\textsuperscript{4,5}, they are still limited and prevent metabolic engineering of this promising organism. While developing such genetic tools, implementation is currently being attempted for a candidate pathway for the production of ethylene glycol.

Future work

Current work focuses on developing the genetic tools necessary for metabolic engineering in M. thermoacetica. If ethylene glycol can be produced from the chosen pathway, further downstream engineering, such as gene deletions, will be performed to increase yield. Pathways for other target products will also be introduced in M. thermoacetica to further demonstrate its importance as a chassis organism. This work will also strengthen our knowledge on M. thermoacetica and its metabolism.

REFERENCES

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