ERA CoBioTech

BIOTECH RESEARCH AND INNOVATION HACK 2021

Kick Off of the 3. call projects of ERA CoBioTech

Synthetic Biology for Sustainable Production of the Methionine Analogon HMTB

SynBioMet

Prof. Thomas Walther

SynBioMet

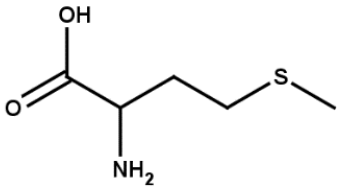
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant 722361

27.09.2021

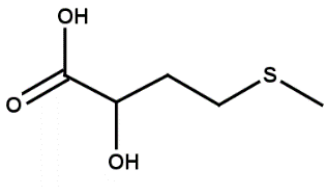
Project partners

- Partners:
  - Institute of Natural Materials Technology, Technische Universität Dresden, GERMANY
  - Toulouse Biotechnology Institute, INSA Toulouse, FRANCE
  - ESPCI, FRANCE
  - Adisseo, FRANCE
- Total project budget: 1.500.000 €
- 01/06/2021 – 31/05/2024

- Project objectives



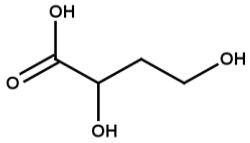
METHIONINE



HMTB
(Methionine-Analogon)

Application:	Supplements in poultry diets
Market volume:	1.6 Mt/year
Annual growth:	>5 %
Production:	chemically from petrol and natural gas

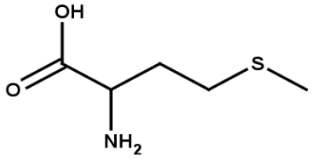
Introduction

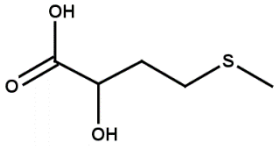


(L)-2,4-DHB

+ CH_3SH
Chemical synthesis,
100 % yield

METHIONINE





HMTB
(Methionine-Analogon)

Technological problems
Incorporation of sulfur is metabolically costly
-> max yield 0.6 g/g – 0.9 g/g

Maximum solubility: 50 g/L

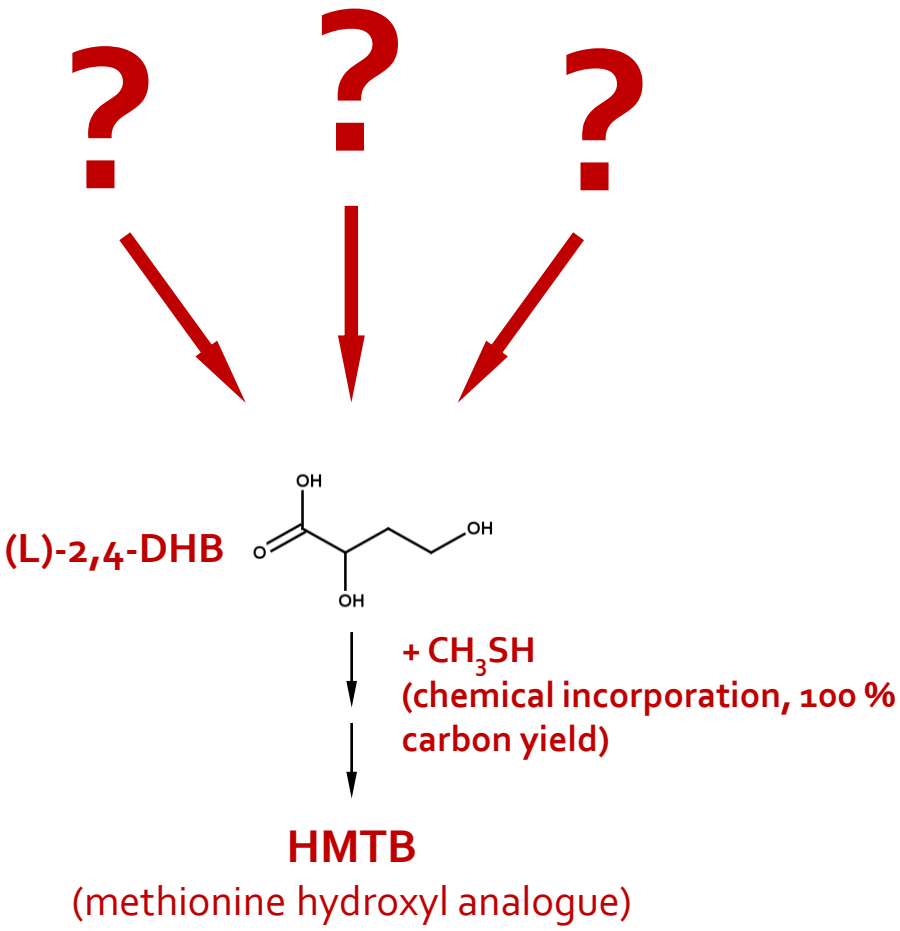
Solution
2-stage bio/chemical synthesis
-> max yield 1.2 g/g

Maximum solubility of DHB/HMTB > 150 g/L

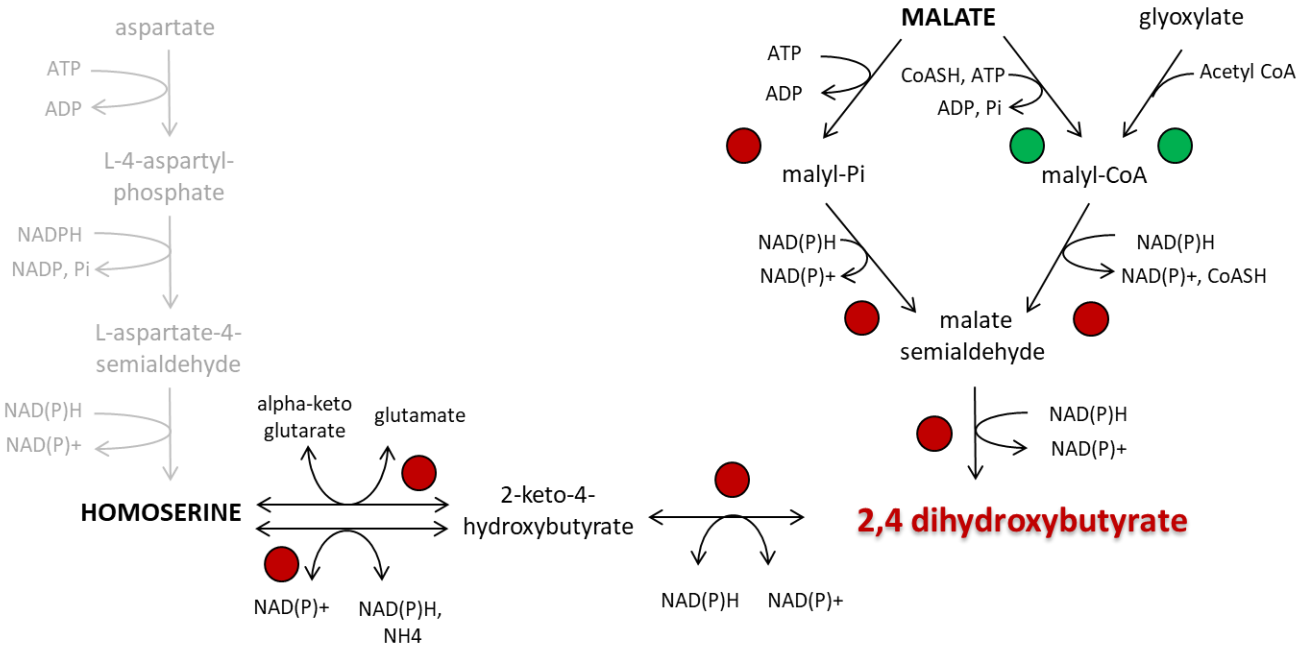
Introduction

DHB from petrol is too expensive

DHB is not a natural metabolic intermediate

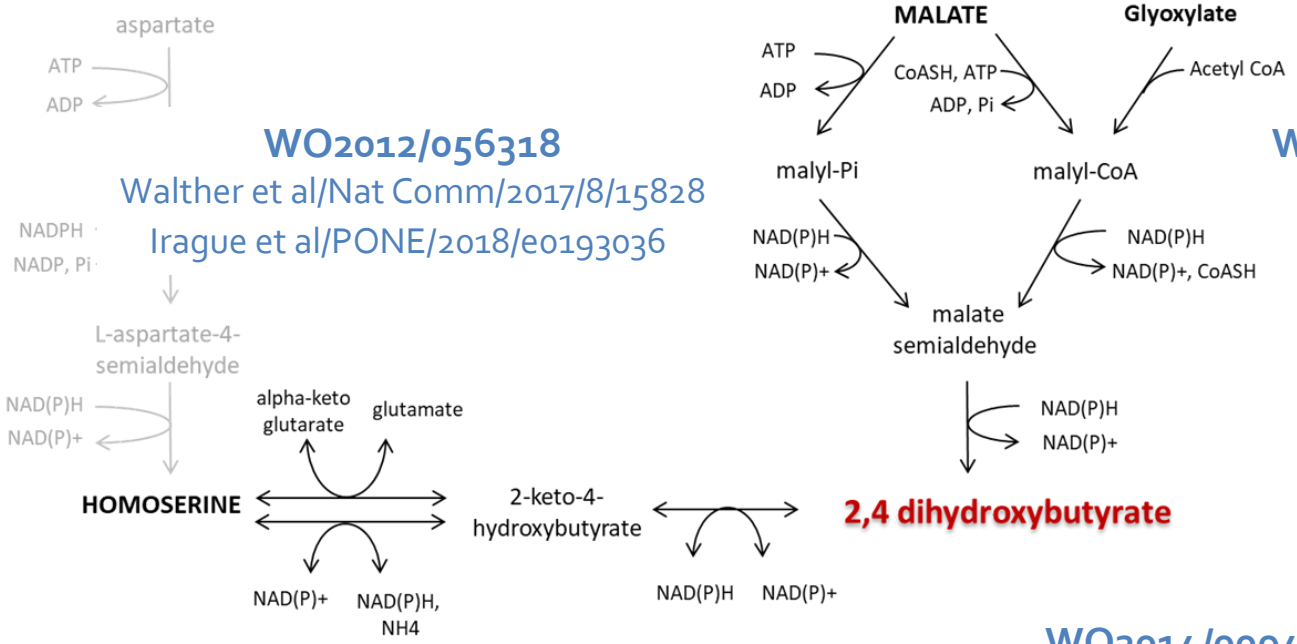


Introduction



Implementation of synthetic DHB pathways required massive enzyme and strain engineering

Introduction



WO2012/056318

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Irague et al/PONE/2018/e0193036

WO2013/160762

WO2014/009435

Walther et al/Metab Eng/2018/45/237-245

Frazao et al/Biochem J/2018/475/3887-3901

Introduction

- Published strain/process performance:
  DHB yield: 0.1 g/g in non-optimized producer strain in 24 h
  Product titer: 8 g/L

- Process performance of molecules in same price range
  Yield > 0.5 g/g
  Productivity > 2 g/L/h
  Product titer > 150 g/L

-> Gap between observed and industrially relevant performance

Introduction

Project objectives

- Development of a microbial fermentation process for the biosynthesis of 2,4-dihydroxybutyric acid (DHB)

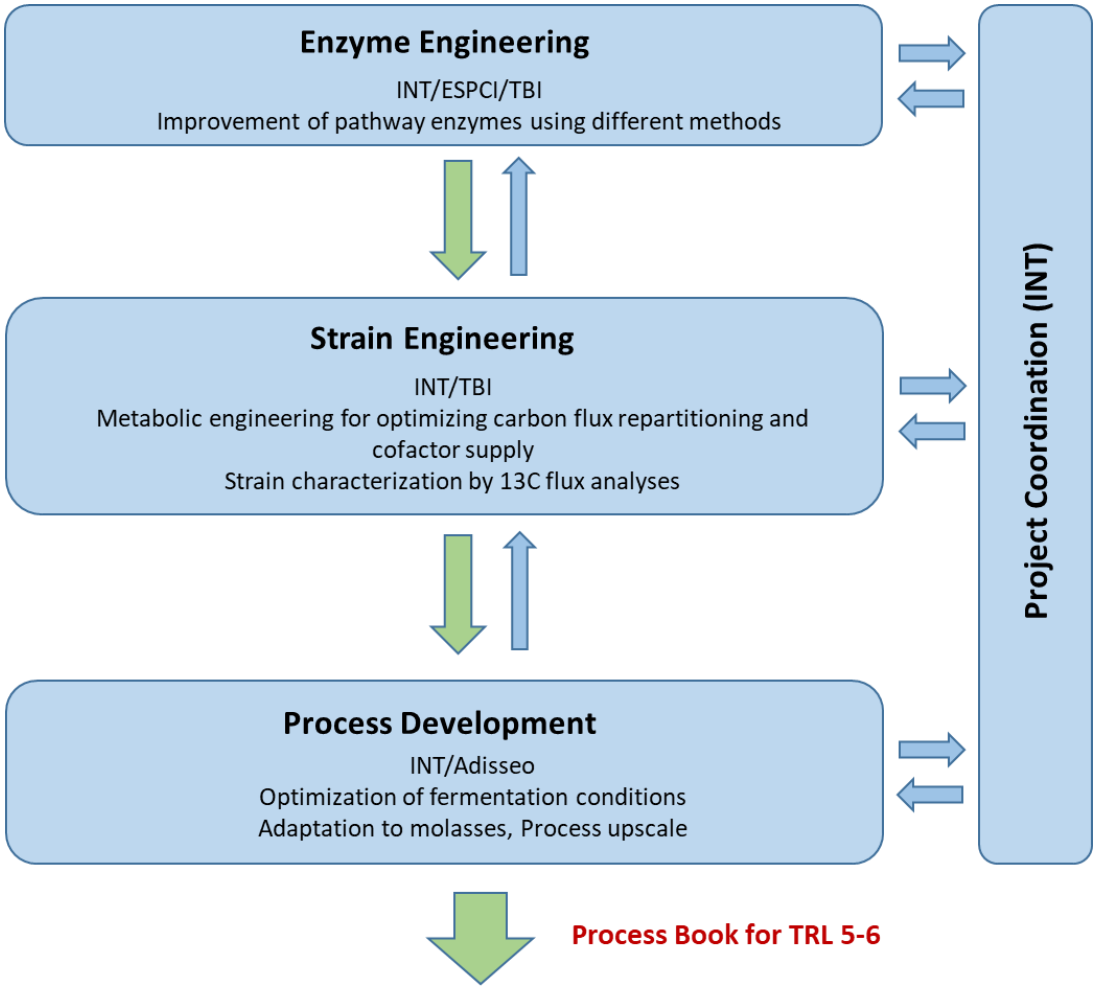
-> Attain industrially relevant DHB yields and productivities

- Improvement of enzymatic activities in synthetic metabolic pathways
- Optimization of producer strains
- Optimization of the fermentation process

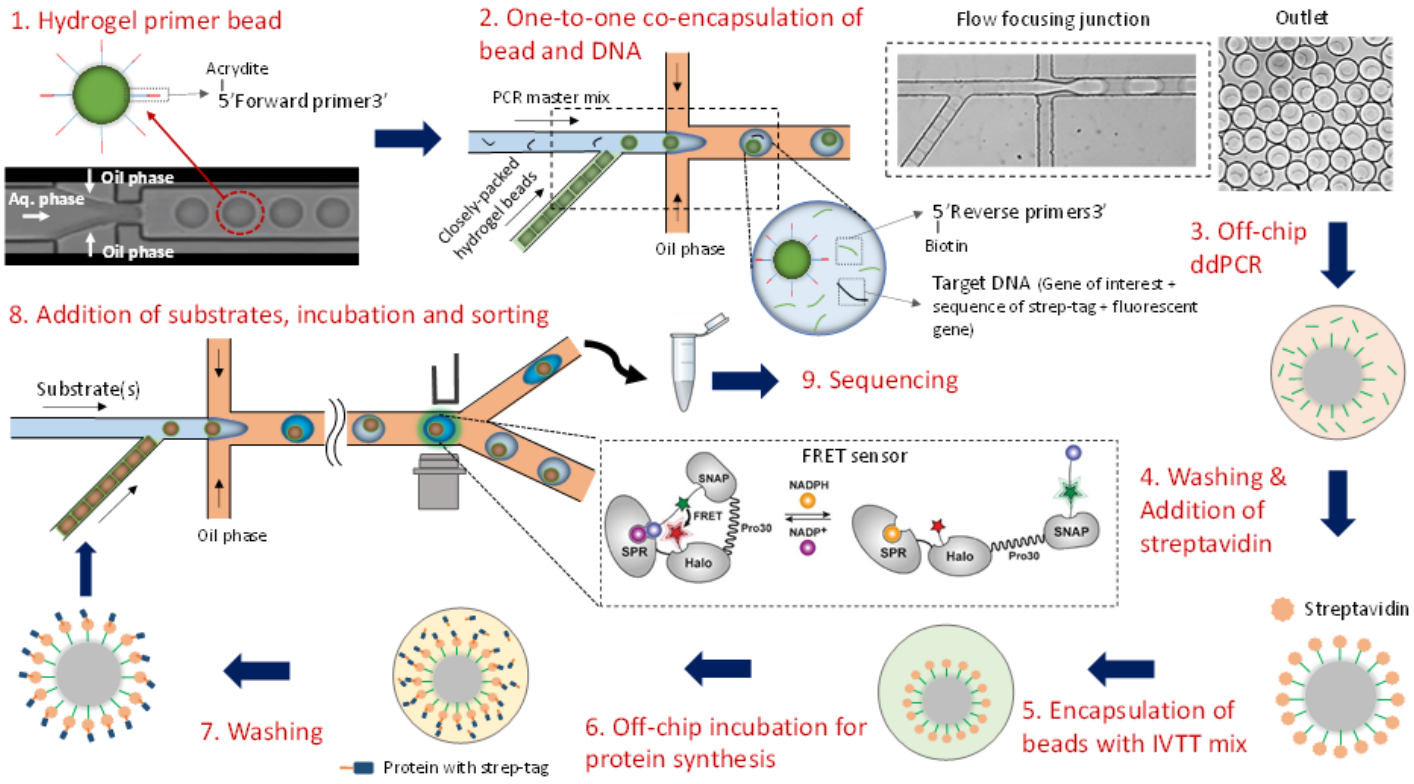
Scientific approach and project topic area

- Synthetic Biology/Systems biology/Applied biotechnology
- Enzyme engineering, Metabolic engineering, Fermentation technology

Project plan



- Highlight: Microfluidics-based enzyme engineering



Project plan

- Highlight: Microfluidics-based enzyme engineering

- cell-free expression of mutant enzymes alleviates the transformation efficiency barrier present in conventional screenings

- Together with the analysis of mutant enzymes in microfluidic device, this gives rise to unprecedented throughput

Expected outcomes

- *Outcomes*

- Develop strains which produce DHB at industrially relevant titers and yields in an industrially relevant environment (TRL 5-6)
- High-performing cell-free enzyme expression and screening system based on microfluidics platform

- *Planned implementation and exploitation of results*

- DHB producer strains shall be used by the industrial partner Adisseo
- Enzyme screening system will be a valuable tool for the entire Synthetic Biology community

Contact details

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