ERA CoBioTech

BioTech Research & Innovation Hack

2021

ERA CoBioTech Funded Projects at A Glance: INDIE

Biotechnological production of sustainable indole

PART OF EUROPEAN BIOTECH WEEK

INNOVATION IS IN OUR GENES

INDIE

Biotechnological production of sustainable indole

The INDIE project aims to produce indole via microbial fermentation and enzymatic bioconversion. In our project, we use the bacterium Corynebacterium glutamicum for the sustainable production of indole because it is capable of producing high amounts of the amino acid L-tryptophan, a direct precursor of indole.

The INDIE objectives

Indole is an important flavouring compound with the main market in dairy, tea drinks and fine fragrances. Pure indole, at low concentrations, exhibits a floral odour characteristic of jasmine. Currently, indole is mainly isolated from coal tar. Natural indole is prepared by conversion of natural tryptophan, which is a costly procedure. There is a strong demand for a more cost-efficient method for preparing natural indole, avoiding chemistry and with improved sustainability. In the INDIE project academic partners from Wageningen Plant Research (NL) and Wageningen University - Systems and Synthetic Biology (NL), Bielefeld University - Biology and Center for Biotechnology (DE), and the National Institute of Biology, Department of Biotechnology and Systems Biology (SI) work together with Axxence Aromatic GmbH (DE), a company manufacturing natural aroma chemicals, with the aim to produce sustainable indole using fermentation and biocatalysis approaches.

The INDIE approach

INDIE combines synthetic and systems biology with bioinformatics for establishing sustainable bioproduction of natural indole. An environmental-friendly production process will be chosen in combination with non-food competitive and renewable substrates, which will be at the same time cost effective. The approach to achieve a biotechnological production of indole is based on the principle of design-build-test-learn-cycle inherent to systems and synthetic biology approaches. A metabolic model, describing all biochemical pathways of *C. glutamicum* is used to design a bacterium that can produce indole in an optimal way. On the other hand, the most efficient biosynthetic enzymes were recruited by mining of sequence databases from various sources (plants, bacteria). The design was further tuned by using observations on the bacterium as a system, meaning that regulatory bottlenecks and unintended side products are eliminated. For this purpose, we have designed regulatory circuits that guarantee optimal flow of the metabolism to indole. The best indole-producing strains developed in this way are tested in an industrial setting, to produce flavour-grade indole. All experimental data is managed using FAIR principles.

Main results

Natural indole is produced by plants as a released volatile, and can be found in, for instance, jasmine and neroli essential oils. In maize, indole was shown to be an essential herbivore-induced volatile priming signal. Some bacteria are able to produce small amounts of indole. Indole acts as an extracellular signal molecule, influencing various aspects of bacterial physiology, and has a toxic effect on cells in higher concentrations.

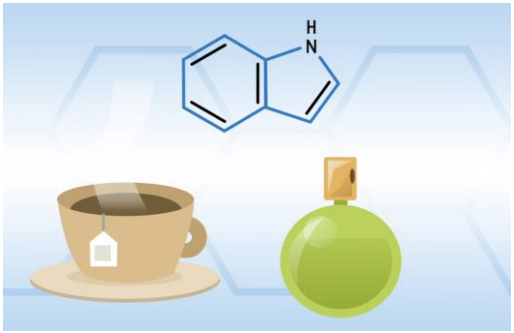

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Figure 1: Indole applications

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Consortium:

Bielefeld University (Germany)

Wageningen University (The Netherlands)

National Institute of Biology (Slovenia)

Axxence Aromatic GmbH (Germany)

Project duration:

1 May 2018 - 31 March 2022

Total budget: 1.0 €M

This project has received funding from the European Union´s Horizon 2020 research and innovation programme under grant agreement No [722361]

The INDIE consortium already gained high expertise on metabolic engineering of the tryptophan biosynthetic pathway, especially on strain engineering enabling optimized provision of anthranilate as precursor for indole production. Moreover, deep insights into chemical and gene regulatory effects by indole, will guide efforts to develop a fermentative indole production processes in the future.

Future prospect

Indole is an important flavouring compound with a market size of 30 million €/year. It is currently mainly produced from coal tar or is synthesized by a variety of multi-step chemical conversions. The fermentative production will lead to a more cost-efficient method for preparing natural indole, avoiding chemistry and with improved sustainability. More broadly, the computational models and biosynthetic and regulatory building bricks generated in INDIE will be recruited to build a systems and synthetic biology framework for Corynebacteria that will be easily extendable to new food ingredients derived from aromatic amino acids, thereby strengthening the potential of these bacteria for sustainable aromatic compound production. INDIE will accelerate technology transfer to the European level, hence opening new markets and strengthening European efforts to achieve sustainable industrial development.

Up to now, the INDIE project published eight scientific papers in peer reviewed journals.
https://doi.org/10.3390/microorganisms9040824
https://doi.org/10.3390/microorganisms8121945
https://doi.org/10.3390/microorganisms8060866
https://doi.org/10.1007/978-3-030-39267-3_10
https://doi.org/10.1002/biot.201900451
https://doi.org/10.1007/978-3-030-31897-0_4
https://doi.org/10.1016/j.copbio.2019.09.011
https://doi.org/10.1016/j.ymben.2019.03.008
https://tinyurl.com/BiotechData (paper describing data management approaches developed and used in this project, in Slovenian)
https://tinyurl.com/FascinatingPlants (children's book with experiments that can be done at home or in classroom, in Slovenian).

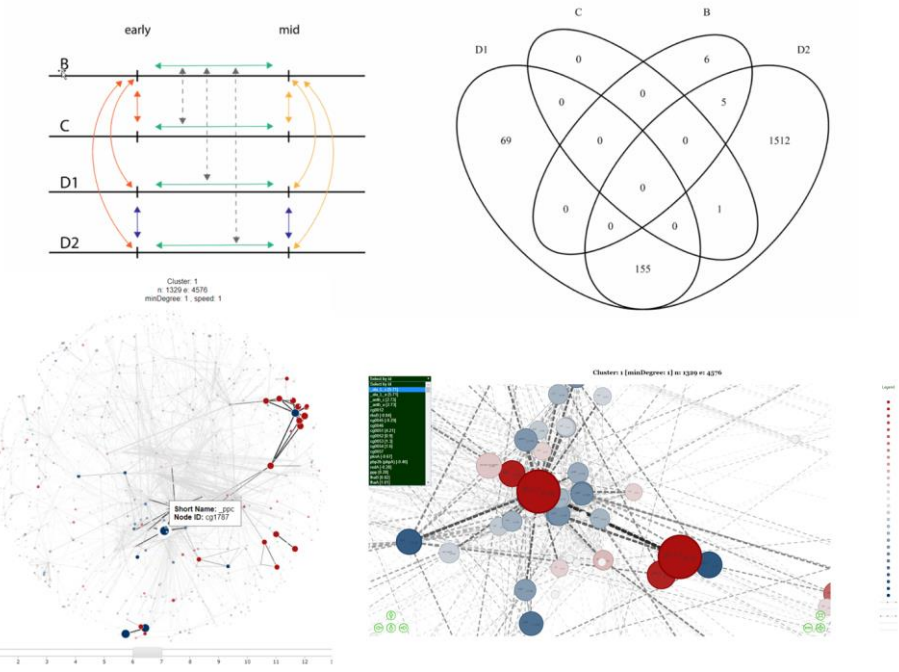

Figure 2: Systems biology analysis of indole production

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Figure 3: Production of indole in bioreactors

Figure 4: INDIE researchers meeting in Slovenia

Website: https://indie.cebitec.uni-bielefeld.de/
Twitter: @INDIEbiotech
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