

De novo* curcumin biosynthesis by an engineered *Saccharomyces cerevisiae

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Curcumin, the major active compound found in *Curcuma longa*, is extensively studied as a natural cancer-fighting drug. However, curcumin accumulates in low amounts over long periods and its extraction process is costly and inefficient. In addition, its chemical synthesis is complex. Curcumin biosynthesis starts with the phenylpropanoid pathway, whose reactions convert the aromatic amino acids to the curcumin precursor ferulic acid. Subsequently, ferulic acid is converted to curcumin by 4-coumarate-CoA ligase and by type III polyketide synthases (PKSs) using malonyl-CoA as extender substrate. Herein, we developed for the first time a genetically engineered *Saccharomyces cerevisiae* strain capable of *de novo* curcumin biosynthesis. CRISPR-Cas9 was used to integrate the biosynthetic pathway. Initially, curcumin production was evaluated from supplemented ferulic acid. The highest curcumin yields were obtained using a bacterial feruloyl-CoA synthetase and type III PKSs from *C. longa*. Afterwards, the enzymes responsible for the conversion of *p*-coumaric acid into ferulic acid were expressed in a tyrosine and *p*-coumaric acid overproducing *S. cerevisiae* strain. The enzymes included 4-hydroxyphenylacetate 3-hydroxylase subunits from bacteria and caffeic acid *O*-methyltransferase from *Arabidopsis thaliana*. After confirming the ferulic acid biosynthesis, the other enzymes responsible for curcumin biosynthesis were expressed in this strain. Other modifications are also being performed to increase yields including increasing of the precursor supply and the deletion of competing pathways.

List of flash poster presentations

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1	Long-read direct RNA sequencing of the mitochondrial transcriptome of <i>Saccharomyces cerevisiae</i> as a method to study polycistronic expression and splicing	Charlotte Koster, Delft University of Technology, Netherlands
2	<i>De novo</i> curcumin biosynthesis by an engineered <i>Saccharomyces cerevisiae</i>	João Rainha, Centre of Biological Engineering, University of Minho, Portugal
3	Aerobic overproduction of pyruvate and derived biochemicals in <i>Pseudomonas putida</i> engineered for accelerated co-utilization of cellulosic sugars	Pavel Dvořák, Masaryk University, Czech Republic
4	A novel Cas3 base-editor for efficient directed evolution of complex metabolic pathways in <i>S. cerevisiae</i>	Anna Zimmermann, KULeuven, VIB, Belgium
5	Synthetic biology approaches and biochemical biodiversity towards Glucobrassicin production in <i>Saccharomyces cerevisiae</i>	Letizia Maestroni, University of Milano-Bicocca, Italy
6	Sharing is caring: the benefit of a bistable matrix expression	Jolien Meesters, KU Leuven, Belgium
7	New-to-nature biological sensors: unlocking the full potential of biological sensors beyond nature	Brecht De Paepe, Centre For Synthetic Biology - Ghent University, Belgium
8	Angels or demons in the fight against Salmonella: the double edged sword of probiotics in the poultry industry.	Lene Jacobs, KU Leuven, Belgium
9	Sensbio: an online server for biosensor design	Jonathan Tellechea, Universitat Politècnica de Valencia, Spain
10	Upscaling the production of a monomer for bio-based plastics from lignin	Jan Notheisen, Institute of Biochemical Engineering, University of Stuttgart, Germany
11	Engineering the yeast <i>Kluyveromyces marxianus</i> for production of aromatic flavours and fragrance molecules	Joel Akinola, University College Cork, Ireland
12	Developing a synthetic regulatory network for non-native substrate assimilation	Cláudia Vicente, Toulouse Biotechnology Institute, France
13	Unlocking the potential of chitin-rich waste for the production of specialty sugars	Sofie Snoeck, University of Ghent, Belgium
14	Design frameworks for engineering efficient cell factory performance within host and industrial constraints	Alexander Darlington, University of Warwick, United Kingdom
15	Using Triplex-Forming Oligos (TFOs) to repress promoter activity in Chinese Hamster Ovary (CHO) cells	Mohamed Hussein, ACIB/ BOKU, Austria