

# Computational design of yeast-based cell factories

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## Summary

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*The current study aims to use advanced modeling approaches where genome-scale models are combined with enzymatic and thermodynamic constraints, to understand the growth laws and energy metabolism of various Crabtree positive and -negative yeast strains.*

Research field:	Chemistry and Biotechnology
Supervisors:	Petri-Jaan Lahtvee Isma Belouah
Availability:	This position is available.
Offered by:	School of Science Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between May 03, 2021 00:00 and May 31, 2021 23:59 (Europe/Zurich)

## Description

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The transition towards bioeconomy requires novel processes that use sustainable substrates, have improved life cycle assessments, and, hence, require less energy to produce. Here, microbial cell factories have a pivotal role in enabling the sustainable and climate-neutral bio-manufacturing of food and feed ingredients, chemicals, fuels, enzymes, medicines, and other novel materials. Understanding how and why cells organise their metabolism and therefore fluxes through the metabolic network in a specific way is a key question in metabolic research. Such understanding is highly relevant from a fundamental point of view but also crucial for various applications in biomedicine and biotechnology.

The current project is interested in studying three distinct yeast strains with diverse growth characteristics to better understand their underlying growth laws. The non-conventional Crabtree negative yeasts *Rhodotorula toruloides* and fast-growing *Kluyveromyces marxianus* will be studied and compared with the model yeast *Saccharomyces cerevisiae*. In our previous research, we have sequenced the *R. toruloides* strain, developed metabolic engineering tools (CRISPR/Cas9, Golden Gate Assembly), and developed a systems biology platform with a genome-scale model and omics data analysis pipelines. The model will be utilised to design efficient pathways for the yeast *R. toruloides* to consume lignocellulosic sugars and convert them into value-added chemicals, e.g. antioxidants. The model predictions will be validated via metabolic engineering of *R. toruloides*.

### Responsibilities and tasks:

- Develop thermodynamics and enzyme constraint models for the non-conventional yeast *R. toruloides*
- Compare the developed models with the existing thermodynamic models of *S. cerevisiae* and enzyme-constrained models of *K. marxianus*.
- Design *R. toruloides* cells to accumulate and secrete antioxidants
- Overexpress native pathways in *R. toruloides* for improved CO<sub>2</sub> fixation

### The applicant should fulfil the following requirements:

- MSc degree in synthetic biology, biotechnology, microbiology, or similar field
- Previous experience in working with microbes
- Previous experience in metabolic modeling
- Previous experience in metabolic engineering is a plus

- Previous experience with yeast is a plus



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