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Sugar pathways in fungi and metabolic engineering as a tool for biochemical production

Currently the production of a vast majority of fuels and chemicals is still based on crude oil. Depletion of fossil fuels and the concern about carbon dioxide emissions are issues needing serious attention in the near future. Therefore alternative, more sustainable ways for efficient production of fuels and chemicals are needed. An ideal way for production would be a Biorefinery based on waste materials.

Many of the desired chemicals to be produced by microbes used as production hosts in Biorefineries are not needed by the microbe; therefore they are not produced at all or the production yields are not sufficient enough for industrial purposes. To increase production rates or to produce new compounds metabolic engineering of the host organism is needed. New pathways providing the enzymes to convert the raw material to the desired chemical can be introduced to host cells, or pathways already existing can be boosted up, or attenuated to redirect the carbon provided. In order to be able to engineer the cells, profound understanding of the host metabolism is needed. Genes expressing the enzymes of various metabolic pathways need to be characterized and regulators behind the repression and activation mechanisms need to be unravelled.

Host selection is an important consideration in developing production organisms for Biorefineries, and fungi are often preferred as they possess many desired properties. Yeast *Saccharomyces cerevisiae* is well known as an ethanol producer and methods to engineer it are well in place. It has many advantages in organic acid production as it naturally excretes many of them, besides being remarkably acid tolerant. Low pH is an advantage as purification of undissociated forms of organic acids is cheaper. Low pH in bioreactors also prevents contaminations. In addition to *S. cerevisiae* filamentous fungi can be used as production hosts. *Aspergillus niger* for instance is a well-known citric acid producer and its capability of using a great variety of different carbon sources can be exploited in many ways in organic acid production.

Lignocellulosic biomass consists mainly of hexose sugars as glucose and pentose sugars as D-xylose and L-arabinose but also more rare sugars as D-galactose and L-rhamnose. The catabolic pathways for the main components are relatively well known but especially the details of the metabolism of rare sugars needs still more research as not all the genes encoding enzymes acting in the catabolic pathways are known. For efficient conversion of biomass into chemicals it is important to address the conversion of all carbohydrates the provided biomass contains.

The goal of my PhD thesis is to gain deeper understanding of the D-galactose and L-rhamnose metabolic pathways in fungi, more specifically in yeast *S. cerevisiae* and *Scheffesomyces* (*Pichia*) *stipitis* and the filamentous fungus *A. niger*. Moreover, the aim is to exploit yeast as a cell factory for production of acids, finding applications in polymer industry.

Selected publications

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