Establishing Saccharomyces cerevisiae as platform for isoprenoid production

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Directed Evolution towards Increased Isoprenoid Production in Saccharomyces cerevisiae

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Introduction

Organic synthesis of isoprenoids often results in low yields due to their complex structure. This makes production in large scale, by organic synthesis economically unfeasible. Microbial production can easily be scaled to meet current demands and it is also an environmental benign production method compared to organic synthesis. Thus it would be attractive to engineer a microorganism to produce high amounts of IPP and other immediate prenyl precursors such as geranyl pyrophosphate, farnesyl pyrophosphate and geranylgeranyl pyrophosphate, thereby establishing it as a microbial platform for heterologous expression of isoprenoid genes (see figure 1).

This project is focused on creating diversity within a lycopene producing S. cerevisiae strain by construction of gDNA-, cDNA-, and transposon-libraries. The diversified population of S. cerevisiae clones will afterwards be screened using the isoprenoid molecule lycopene as a model compound, hereby enabling the isolation of phenotypes producing higher amounts of isoprenoid. This will elude novel genetic targets for increasing isoprenoid production in S. cerevisiae.

Future perspectives

When different genetic perturbations that increase the production of isoprenoids have been identified, the underlying metabolic mechanisms will be sought identified through further analysis. We foresee that some perturbations will be straight forward to identify e.g. overexpression of genes which are directly linked to isoprenoid precursor biosynthesis. The mechanisms which are harder to unravel will be the ones encoded by ORFs with unassigned functions or regulatory mechanisms. Finally systematic combinations of the identified perturbations will be engineered aiming at the construction of a S. cerevisiae platform for high titer production of isoprenoids.

References