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Title: Strategies to enhance the activity of key enzymatic steps of Isoprenoid Biosynthesis in Saccharomyces cerevisiae

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Abstract:

Mevalonate pathway (MVP) is an essential metabolic pathway present in eukaryotes, archaea, and some bacteria 1. MVP is responsible for synthesizing a diverse class of biomolecules, that involves isoprenoids, cholesterol, and a precursor to many commercially valuable terpenoids. The efforts to exploit this pathway for value-added product biosynthesis by expressing the genes in heterologous hosts is being attempted by different groups. Isoprenoids produced from genetically engineered organisms, using renewable carbon source, are the new micro-factories for many sustainable chemical productions. Their capability to replace petroleum-derived production strategies for various terpenoids is a step towards sustainable development 2. However, for the synthetic biological route to succeed, a very efficient production system with an efficient synthesis pathway is required, which is why efforts to enhance the biosynthetic pathways are extensively being worked upon. In MVP, converting HMG Co- A into mevalonate is a rate-limiting step that requires two molecules of NADPH for reduction. In this thesis, we have attempted to increase the flux by increasing the reaction substrate NADPH by the creation of gene fusions (synthetic metabolon) in the Pentose phosphate pathway, which is a key cytosolic NADPH production pathway. Geranylgeranyl Pyrophosphate (GGPP) is a crucial metabolic hub where the flux is diverted to different branching pathways. In the second part of the thesis, there was an attempt at engineering the GGPP synthase enzyme in order to increase the turnover rate of GGPP production.

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