BRC Science Highlight
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Redirection of the Glycolytic Flux Enhances Isoprenoid Production in *Saccharomyces cerevisiae*

Background/objective

Isoprenoids are a structurally diverse class of organic compounds with applications in biofuels, pharmaceuticals, and other industries. However, efforts to achieve commercial production from engineered microbes have so far fallen short. Here, researchers address a key challenge by increasing the [NADPH]/[NADP+] in *Saccharomyces cerevisiae* by manipulating flux through the oxidative pentose phosphate pathway (PPP).

Approach

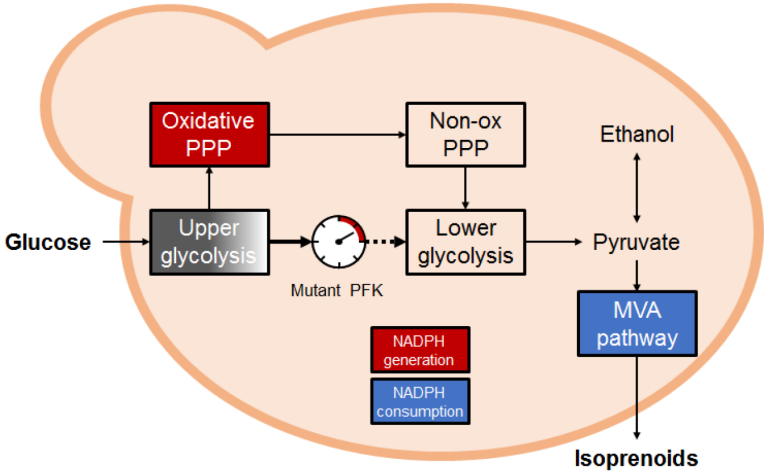
- Implemented a "push-pull" strategy on glucose-6-phosphate (G6P) to increase availability of NADPH: overexpression of ZWF1 and downregulating catalytic activities in upper glycolysis via phosphofructokinase (PFK) mutations.
- The strategy was tested for the production of amorphadiene, a candidate sesquiterpene isoprenoid.

Results

- The combination of ZWF1 overexpression and PFK mutations resulted in an increase in [G6P] and, subsequently, in [NADPH]/[NADP+].
- This strategy increased amorphadiene titers by at least 1.6 times over that achieved in other previously engineered strains.

Significance

The strategy demonstrated here will contribute to the economically feasible production of isoprenoids and other bioproducts that rely on NADPH or other intermediates from upper glycolysis.



NADPH production in *S. cerevisiae* was enhanced by increasing availability of the gateway metabolite of the oxidative PPP. This strategy increased the production of amorphadiene, an NADPH-dependent isoprenoid.

*Kwak et al. 2019. "Redirection of the Glycolytic Flux Enhances Isoprenoid Production in Saccharomyces cerevisiae." **Biotechnology Journal.** DOI:*10.1002/biot.201900173.

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