

# METABOLIC ENGINEERING OF *SACCHAROMYCES CEREVISIAE* FOR HIGH LEVEL PRODUCTION OF AROMATIC CHEMICALS

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The synthesis of functional plant natural products using microbial hosts is considered a safe, cost-competitive and sustainable approach to their production. In particular, the budding yeast has attracted much attention due to its superior ability to express the cytochrome P450s common in downstream of plant pathways for production of these high-value compounds. However, aromatic amino acid (AAA)-based production in yeast is an outstanding challenge. Here we present the construction of a *Saccharomyces cerevisiae* platform strain able to produce *p*-coumaric acid, a common precursor for many commercially valuable chemicals. We demonstrate that carbon flux can be rewired from glycolysis directly to erythrose 4-phosphate formation, enabling an increase in production of AAAs and their derivatives. Through systematic removal of bottlenecks in the AAAs biosynthesis pathway and further optimizing carbon distribution between glycolysis and AAAs biosynthesis pathway by using a promoter library screening approach, *p*-coumaric acid production increased to about 3 g l<sup>-1</sup> under shake flask conditions, with ~ 15% conversion yield on glucose. Furthermore, the engineered strain produced up to 12.5 g l<sup>-1</sup> of *p*-coumaric acid under fed-batch fermentation conditions, the highest reported titre for aromatic chemicals produced in yeast. The strategies presented here can also be applicable to other microorganisms for production of aromatic chemicals.