High-yield resveratrol production in genetically modified Escherichia coli via L-tyrosine

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Abstract: Resveratrol is one of the most widely studied representatives of the plant-produced polyphenols. Plant polyphenols have been the subject of several recent scientific investigations since many of the molecules in this class have been found to be highly active in the human body, with a plethora of health-promoting activities against a variety of diseases, including heart disease, diabetes, and cancer, and even with the potential to slow down aging. Escherichia coli with the advantages like simple genetic background, short cultivate time and relatively higher yield, we set out to produce resveratrol in microbial systems as an alternative to extraction from plant or chemical synthesis. In this study, E. coli was engineered for the production of resveratrol using tyrosine as the initial precursor of the pathway. The pathway design included tyrosine ammonia lyase (TAL) from Rhodotorula glutinis to convert tyrosine to p-coumaric acid and stilbene synthase ligase (STS) from Vitis vinifera, a 4-coumaroyl:CoA ligase (4CL) from Arabidopsis thaliana to convert p-coumaric acid to resveratrol. The genes were codon-optimized and different combinations of plasmids were used to improve the titer of resveratrol. TAL was able to efficiently convert 8 mM of L-tyrosine to resveratrol with the highest production obtained being 759 mg/L. Finally, the highest resveratrol production obtained using TAL, STS and 4CL was 2,325 mg/L.

Keywords: Resveratrol; E. coli; Polyphenol; L-tyrosine