246a Increasing Flavonoid Production by Metabolic Pathway Engineering in Multiple Yeast Hosts

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Flavonoids are a class of secondary metabolites derived from the plant phenylpropanoid pathway. Many flavonoids exhibit powerful anti-microbial, anti-inflammatory, and anti-carcinogenic effects. Apigenin and chrysin are two flavonoids which inhibit cell growth and induce apoptosis in many human cancers. The biosynthesis of apigenin and chrysin was achieved the first time in Saccharomyces cerevisiae by the construction of the phenylpropanoid pathway in the host strain WAT11U. The functional pathway involves the co-expression of five or six heterologous enzymes in S. cerevisiae. When the entire pathway was engineered into a single host, the concentrations of apigenin and chrysin after 47 hours induction were 430 and 80 μg L-1, respectively. To increase the yield of apigenin, we separated the phenylpropanoid pathway in multiple yeast hosts, in which enzyme expression levels could be increased. Eight strategies with different combinations of yeast hosts expressing portions of the phenylpropanoid pathway were proposed and experimentally investigated. One combination of two strains produced the highest concentration of apigenin (10.5 mg L-1), which was 24-fold higher than five enzymes expressed in a single host. Moreover, our results demonstrated that each of the other strategies significantly increased the apigenin concentration. We discuss the current limitations on the product yield and potential solutions to overcome them.