Rational metabolic engineering and flux optimization enables efficient production of fumaric acid

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An important C4 dicarboxylic acid, fumaric acid(FA) was efficiently produced in *Escherichia coli* by rational metabolic engineering and flux optimization. The initially engineered strain, CWF4N overexpressing PPC, produced 5.30 g/L of FA. To optimize PPC flux, 24 types of synthetic PPC expression vectors were constructed and screened to finally give 5.72 g/L of FA with a yield of 0.432 g/g glucose. The yield was further increased upto 0.493 g/g glucose by overexpressing sdhCDAB. Additionally, CS was combinatorially overexpressed with PPC giving 48 types of synthetic vectors. As a result, 6.24 g/L of FA was produced with a yield of 0.500 g/g glucsoe. Fed-batch fermentation with this final strain gave 25.5 g/L of FA with a yield of 0.366 g/g glucose. Thus, *aspA* gene was deleted and aspartic acid was supplemented to give final titer of 35.1 g/L with a yield of 0.490 g/g glucose. (This works was supported by the Technology Development Program to Solve Climate Changes on Systems Metabolic Engineering for Biorefineries from the Ministry of Science, and ICT through the National Research Foundation (NRF) of Korea (NRF-2012M1A2A2026556) and NRF-2012M1A2A2026557)).