Metabolic engineering of Corynebacterium glutamicum for high-level production of L-arginine

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Corynebacterium glutamicum was engineered for L-arginine production. Random mutagenesis was first performed to increase tolerance to L-arginine. Then, the *argR* and *farR* genes encoding the arginine operon repressor proteins were inactivated. The PPP flux was strengthened by downregulating the *pgi* gene and overexpressing the *opcA*, *pgl*, *tal*, *tkt*, and *zwf* genes in an operon. Next, the Ncgl1221 gene encoding L-glutamate exporter was inactivated. Also, the expression levels of the *argF* and *carAB* genes were optimized for effective converting L-ornithine to L-citrulline. Finally, the *argGH* operon was overexpressed to overcome the rate-limiting arginine synthesis. For the large-scale production of L-arginine, fed-batch fermentation of the final strain was performed in a 1,500 L bioreactor resulting 81 g/L of L-arginine production. [This work was supported by the Technology Development Program to Solve Climate Changes on Systems Metabolic Engineering for Biorefineries (NRF-2012M1A2A2026556) of the Ministry of Education, Science and Technology (MEST) through the National Research Foundation of Korea.]