Systems metabolic engineering of *C. glutamicum* for the fermentative production of L-arginine

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Industrial amino acids powerhouse *Corynebacterium glutamicum* was engineered for L-arginine production. First, random mutagenesis was performed on *C. glutamicum* to increase tolerance to L-arginine. Next, the arginine operon repressor proteins *argR* and *farR* were inactivated. By downregulating the *pgi* gene and overexpressing the *opcA*, *pgl*, *tal*, *tkt*, and *zwf* genes, PPP flux was strengthened. Subsequently, the *Ncgl1221* gene encoding L-glutamate exporter was inactivated to channel L-glutamate to L-arginine. In addition, *argF* and *carAB* gene expression levels were optimized to convert L-ornithine to L-citrulline. Finally, the *argGH* operon was overexpressed. Fed-batch fermentation of the final strain in a 1,500 L bioreactor resulted in 81 g/L of L-arginine production. The approaches described here will be useful in developing microbes for the production of arginine and its derivatives. [This work was supported by the Technology Development Program to Solve Climate Changes on Systems Metabolic Engineering for Biorefineries from the Ministry of Science, ICT and Future Planning (MSIP) through the National Research Foundation (NRF) of Korea (NRF-2012M1A2A2026556 and NRF-2012M1A2A2026557)]