Production of 5-aminovaleric and glutaric acid by metabolically engineered microorganism

December 20 2012

Combining systems metabolic engineering and downstream process, bio-based production of 5-aminovaleric acid and glutaric acid, important C5 platform chemicals, engineered in Escherichia coli could be demonstrated for the first time.

We use many different types of chemicals and plastics for the convenience of our everyday life. The current sources of these materials are provided from petrochemical industry, using fossil oil as a raw material. Due to our increased concerns on the environmental problems and fossil resource availability, there has been much interest in producing those chemicals and materials from renewable non-food biomass through biorefineries. For the development of biorefinery process, microorganisms have successfully been employed as the key biocatalysts to produce a wide range of chemicals, plastics, and fuels from renewable resources. However, the natural microorganisms without modification are not suitable for the efficient production of target products at industrial scale due to their poor metabolic performance. Thus, metabolic capacities of microorganisms have been improved to efficiently produce desired products, the performance of which is suitable for industrial production of such products. Optimization of microorganism for the efficient production of target bioproducts has been achieved by systems metabolic engineering, which allows metabolic engineering at the systems-level.

5-aminovalic acid (5AVA) is the precursor of valerolactam, a potential building block for producing nylon 5, and can potentially be used as a C5 platform chemical for synthesizing 5-hydroxyvaleric acid, glutaric acid, and 1,5-pentanediol. It has been reported that a small amount of 5AVA is accumulated in *Pseudomonas putida* that has impaired L-lysine catabolism since 5AVA is a natural metabolite of L-lysine catabolism in *P. putida*. However, direct fermentative production of 5AVA has not yet been demonstrated, which might have great potential to open market for C5 chemicals and plastics.

In the paper published in *Metabolic Engineering*, a Korean research team led by Distinguished Professor Sang Yup Lee at the Department of Chemical and Biomolecular Engineering, Korea Advanced Institute of Science and Technology (KAIST), a premier science and engineering university in Korea, together with Dr. Seung Hwan Lee at Korea Research Institute of Chemical Technology (KRICT), a government supported research institute in Korea, and Prof. Si Jae Park at Myongji University in Korea, applied systems metabolic engineering approach to develop recombinant Escherichia coli for the production of 5-aminovaleric acid and glutaric acid, the promising C5 platform chemicals, by fermentation. Firstly, they constructed metabolic pathway to produce 5-aminovaleric acid (5AVA) using L-lysine as a direct precursor by employing two enzymes lysine 2-monooxygenase (DavB) and delta-aminovaleramidase (DavA). Secondly, metabolic pathway for the further conversion of 5AVA into glutaric acid was constructed by employing two more enzymes 5AVA aminotransferase (GabT) and glutarate semialdehyde dehydrogenase (GabD). Recombinant *E. coli* expressing DavB and DavA produced 5AVA using L-lysine as a direct precursor, and recombinant *E. coli* expressing DavB, DavA, GabT, and GabD produced glutaric acid from L-lysine. Finally, the L-lysine biosynthetic pathway of *E. coli* was systematically engineered to produce 5AVA from glucose. As a proof-of-concept demonstration, fermentation of this metabolically engineered *E. coli* strain successfully produced

5AVA from glucose. This study showcases the first microbial process for the production of 5AVA and glutatic acid as C5 platform chemicals by developing microbial strain through systems metabolic engineering.

More information: *Metabolic Engineering* (Elsevier): Park, S.J. et al., Metabolic engineering of Escherichia coli for the production of 5-aminovalerate and glutarate as C5 platform chemicals. dx.doi.org/10.1016/j.ymben.2012.11.011