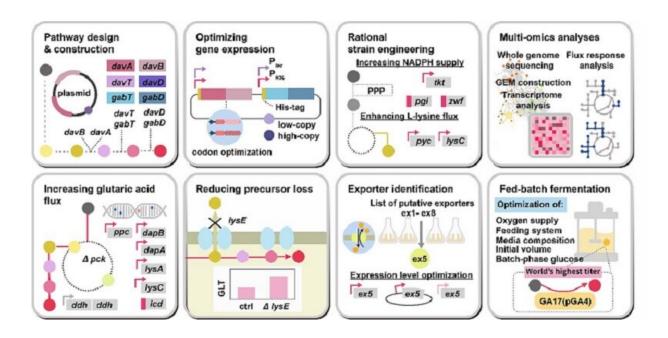


## Engineered C. glutamicum strain capable of producing high-level glutaric acid from glucose

November 17 2020



Systems metabolic engineering strategies employed for the construction of an engineered C. glutamicum strain that is capable of efficiently producing glutaric acid. Credit: The Korea Advanced Institute of Science and Technology (KAIST)

A metabolic engineering research group at KAIST has developed an engineered Corynebacterium glutamicum strain capable of producing high-level glutaric acid without byproducts from glucose. This new strategy will be useful for developing engineered microorganisms for the



bio-based production of value-added chemicals.

Glutaric acid, also known as pentanedioic acid, is a <u>carboxylic acid</u> that is widely used for various applications including the production of polyesters, polyamides, polyurethanes, glutaric anhydride, 1,5-pentanediol, and 5-hydroxyvaleric acid. Glutaric acid has been produced using various petroleum-based chemical methods, relying on non-renewable and toxic starting materials. Thus, various approaches have been taken to biologically produce glutaric acid from renewable resources. Previously, the development of the first glutaric acid producing Escherichia coli by introducing Pseudomonas putida genes was reported by a research group from KAIST, but the titer was low. Glutaric acid production by metabolically engineered Corynebacterium glutamicum has also been reported in several studies, but further improvements in glutaric acid production seemed possible since C. glutamicum has the capability of producing more than 130 g/L of Llysine.

A research group comprised of Taehee Han, Gi Bae Kim, and Distinguished Professor Sang Yup Lee of the Department of Chemical and Biomolecular Engineering addressed this issue. Their research paper "Glutaric acid production by systems metabolic engineering of an Llysine-overproducing Corynebacterium glutamicum," was published online in *PNAS* on November 16, 2020.

This research reports the development of a metabolically engineered C. glutamicum strain capable of efficiently producing glutaric acid, starting from an L-lysine overproducer. The following novel strategies and approaches to achieve high-level glutaric acid production were employed. First, metabolic pathways in C. glutamicum were reconstituted for glutaric acid production by introducing P. putida genes. Then, multi-omics analyses including genome, transcriptome, and fluxome were conducted to understand the phenotype of the L-lysine



overproducer strain. In addition to systematic understanding of the host strain, gene manipulation targets were predicted by omics analyses and applied for engineering C. glutamicum, which resulted in the development of an engineered strain capable of efficiently producing glutaric acid. Furthermore, the new glutaric acid exporter was discovered for the first time, which was used to further increase glutaric acid production through enhancing product excretion. Last but not least, culture conditions were optimized for high-level glutaric acid production. As a result, the final engineered strain was able to produce 105.3 g/L glutaric acid, the highest titer ever reported, in 69 hours by fedbatch fermentation.

Professor Sang Yup Lee said, "It is meaningful that we were able to develop a highly efficient glutaric acid producer capable of producing glutaric <u>acid</u> at the world's highest titer without any byproducts from renewable carbon sources. This will further accelerate the bio-based production of valuable chemicals in pharmaceutical/medical/chemical industries."

**More information:** Taehee Han et al, Glutaric acid production by systems metabolic engineering of an l-lysine–overproducing Corynebacterium glutamicum, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2017483117

## Provided by The Korea Advanced Institute of Science and Technology (KAIST)

Citation: Engineered C. glutamicum strain capable of producing high-level glutaric acid from glucose (2020, November 17) retrieved 25 April 2024 from <u>https://phys.org/news/2020-11-glutamicum-strain-capable-high-level-glutaric.html</u>



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