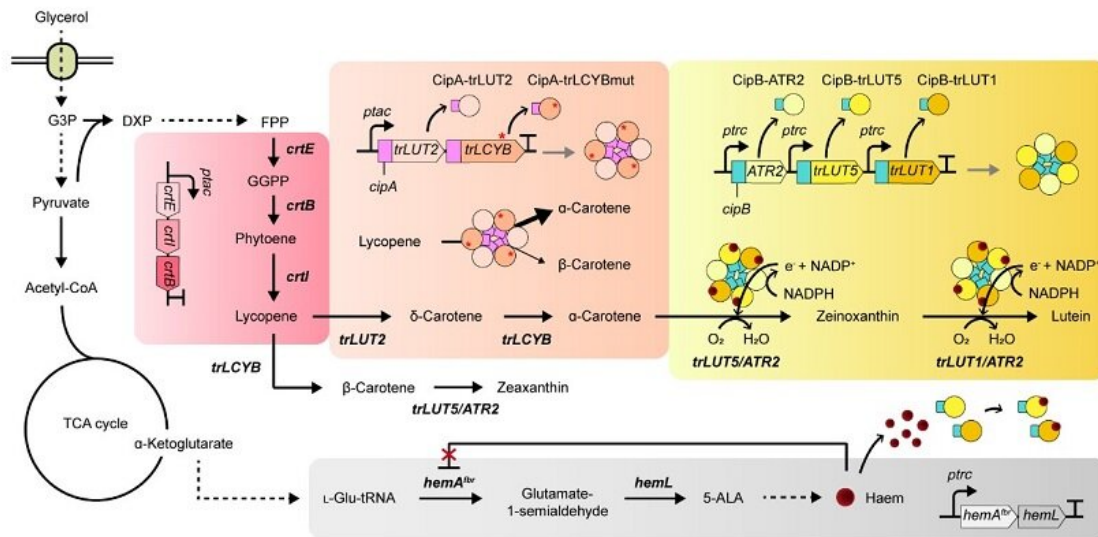


# Metabolically engineered bacterium produces lutein

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Systems metabolic engineering was employed to construct and optimize the metabolic pathways for lutein production, and substrate channeling and electron channeling strategies were additionally employed to increase the production of the lutein with high productivity. Credit: KAIST Metabolic & Biomolecular Engineering National Research Laboratory

Lutein is classified as a xanthophyll chemical that is abundant in egg yolk, fruits, and vegetables. It protects the eye from oxidative damage from radiation and reduces the risk of eye diseases including macular degeneration and cataracts. Commercialized products featuring lutein

are derived from the extracts of the marigold flower, which is known to harbor abundant amounts of lutein. However, the drawback of lutein production from nature is that it takes a long time to grow and harvest marigold flowers. Furthermore, it requires additional physical and chemical-based extractions with a low yield, which makes it economically unfeasible in terms of productivity. The high cost and low yield of these bioprocesses has made it difficult to readily meet the demand for lutein.

These challenges inspired the metabolic engineers at KAIST, including researchers Dr. Seon Young Park, Ph.D. Candidate Hyunmin Eun, and Distinguished Professor Sang Yup Lee from the Department of Chemical and Biomolecular Engineering. The team's study was published in *Nature Catalysis* on August 5, 2022.

This research details the ability to produce lutein from *E. coli* with a [high yield](#) using a cheap carbon source, glycerol, via systems [metabolic engineering](#). The research group focused on solving the bottlenecks of the biosynthetic pathway for lutein production constructed within an individual cell. First, using systems metabolic engineering, which is an integrated technology to engineer the metabolism of a microorganism, lutein was produced when the lutein biosynthesis pathway was introduced, albeit in very small amounts.

To improve the productivity of lutein production, the bottleneck enzymes within the [metabolic pathway](#) were first identified. It turned out that metabolic reactions that involve a promiscuous enzyme, an enzyme that is involved in two or more [metabolic reactions](#), and electron-requiring cytochrome P450 enzymes are the main bottleneck steps of the pathway inhibiting lutein biosynthesis.

To overcome these challenges, substrate channeling, a strategy to artificially recruit enzymes in physical proximity within the cell in order

to increase the local concentrations of substrates that can be converted into products, was employed to channel more metabolic flux towards the target chemical while reducing the formation of unwanted byproducts.

Furthermore, electron channeling, a strategy similar to substrate channeling but differing in terms of increasing the local concentrations of electrons required for oxidoreduction reactions mediated by P450 and its reductase partners, was applied to further streamline the metabolic flux towards lutein biosynthesis, which led to the highest titer of lutein production achieved in a bacterial host ever reported. The same electron channeling strategy was successfully applied for the production of other natural products including nootkatone and apigenin in *E. coli*, showcasing the general applicability of the strategy in the [research field](#).

"It is expected that this microbial cell factory-based production of lutein will be able to replace the current plant extraction-based process," said Dr. Seon Young Park, the first author of the paper. She explained that another important point of the research is that integrated metabolic engineering strategies developed from this study can be generally applicable for the efficient production of other natural products useful as pharmaceuticals or nutraceuticals.

"As maintaining [good health](#) in an aging society is becoming increasingly important, we expect that the technology and strategies developed here will play pivotal roles in producing other valuable natural products of medical or nutritional importance," explained Distinguished Professor Sang Yup Lee.

**More information:** Sang Lee, Metabolic engineering of *Escherichia coli* with electron channelling for the production of natural products, *Nature Catalysis* (2022). [DOI: 10.1038/s41929-022-00820-4](https://doi.org/10.1038/s41929-022-00820-4).  
[www.nature.com/articles/s41929-022-00820-4](https://www.nature.com/articles/s41929-022-00820-4)

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