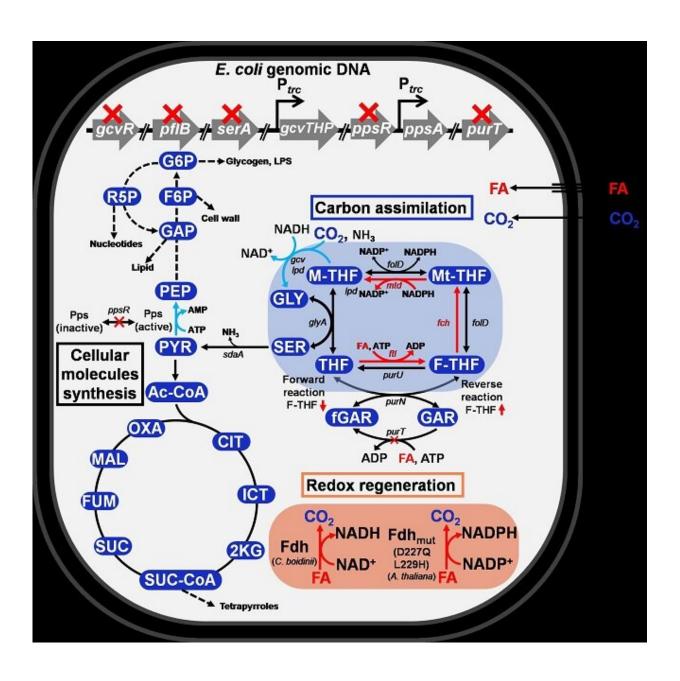


E. coli engineered to grow on carbon dioxide and formic acid as sole carbon sources

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Metabolic engineering strategies and central metabolic pathways of the engineered E. coli strain that grows on CO2 and formic acid. Carbon assimilation and reducing power regeneration pathways are described. Engineering strategies and genetic modifications employed in the engineered strain are also described. Credit: *Nature Microbiology*

Most biorefinery processes have relied on the use of biomass as a raw material for the production of chemicals and materials. Even though the use of CO₂as a carbon source in biorefineries is desirable, it has not been possible to make common microbial strains such as E. coli grow on CO₂.

Now, a metabolic engineering research group at KAIST has developed a strategy to grow an E. coli strain to higher cell density solely on CO_2 and formic <u>acid</u>. Formic acid is a one carbon <u>carboxylic acid</u>, and can be easily produced from CO_2 using a variety of methods. Since it is easier to store and transport than CO_2 , formic acid can be considered a good liquid-form alternative of CO_2 .

With support from the C1 Gas Refinery R&D Center and the Ministry of Science and ICT, a research team led by Distinguished Professor Sang Yup Lee stepped up their work to develop an engineered E. coli strain capable of growing up to 11-fold higher cell density than those previously reported, using CO₂ and formic acid as sole carbon sources. This work was published in *Nature Microbiology* on September 28.

Despite the <u>recent reports</u> by several research groups on the development of E. coli <u>strains</u> capable of growing on CO₂ and formic acid, the maximum cell growth remained too low (optical density of around 1) and thus the production of chemicals from CO₂ and formic acid has been far from realized.



The team previously reported the reconstruction of the tetrahydrofolate cycle and reverse glycine cleavage pathway to construct an engineered E. coli strain that can sustain growth on CO_2 and formic acid. To further enhance the growth, the research team introduced the previously designed synthetic CO_2 and formic acid assimilation pathway, and two formate dehydrogenases.

Metabolic fluxes were also fine-tuned, the gluconeogenic flux enhanced, and the levels of cytochrome bo3 and bd-I ubiquinol oxidase for ATP generation were optimized. This engineered E. coli strain was able to grow to a relatively high OD600 of 7~11, showing promise as a platform strain growing solely on CO₂ and formic acid.

Professor Lee said, "We engineered E. coli that can grow to a higher cell density only using CO₂ and formic acid. We think that this is an important step forward, but this is not the end. The engineered strain we developed still needs further engineering so that it can grow faster to a much higher density."

Professor Lee's team is continuing to develop such a strain. "In the future, we would be delighted to see the production of chemicals from an engineered E. coli strain using CO₂ and <u>formic acid</u> as sole carbon sources," he added.

More information: Junho Bang et al. Escherichia coli is engineered to grow on CO₂ and formic acid, *Nature Microbiology* (2020). DOI: 10.1038/s41564-020-00793-9

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