Enhancing microbe memory to better upcycle excess CO_2

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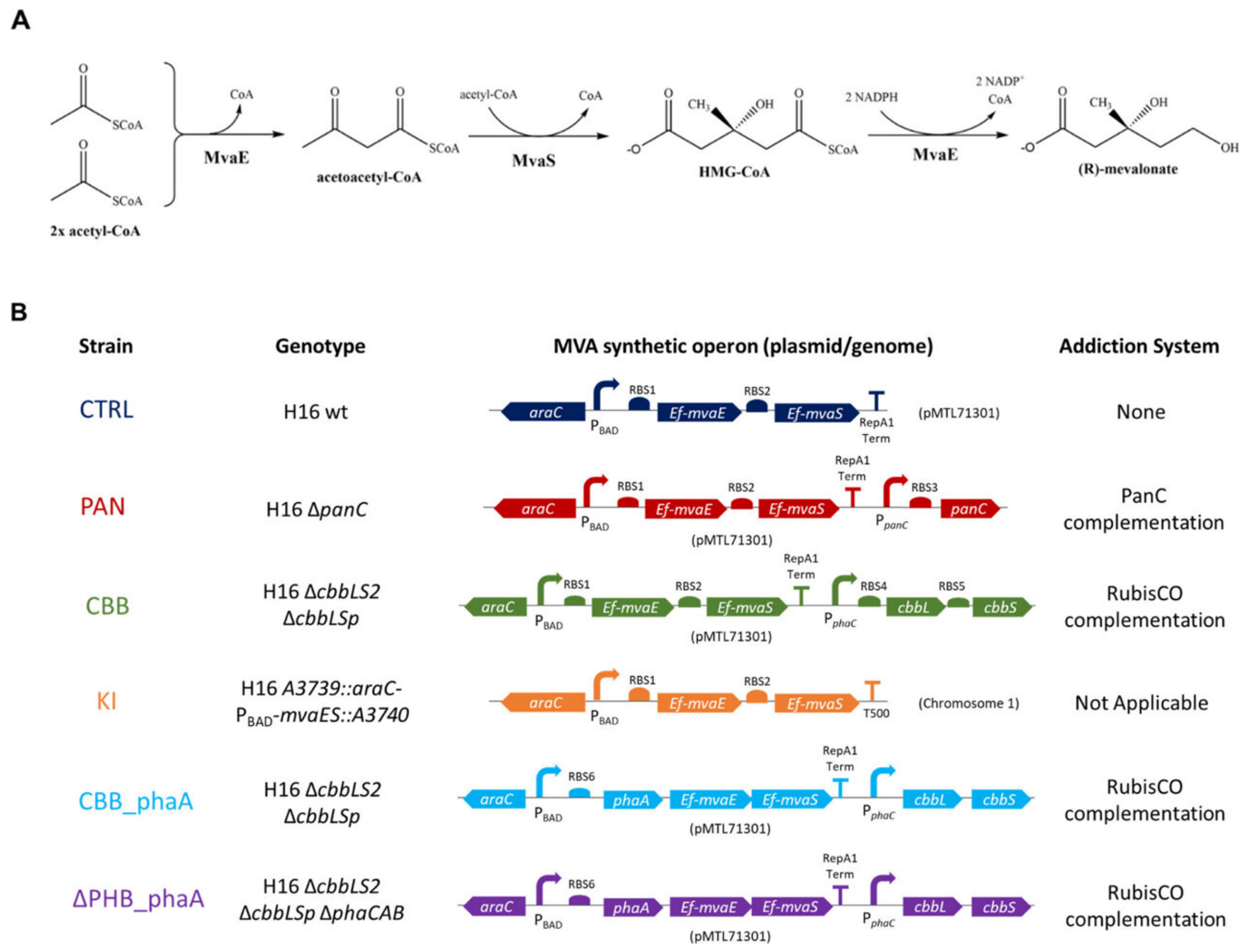

Schematic representation of the upper MVA pathway and summary of the C. necator H16 derivative strains used in this study. Credit: *ACS Sustainable Chemistry & Engineering* (2024). DOI: 10.1021/acssuschemeng.4c03561

While some microbes can make people sick or spoil food, others are critical for survival. These tiny organisms can also be engineered to make specific molecules. Researchers reporting in *ACS Sustainable Chemistry & Engineering* have rewired one such microbe to help tackle greenhouse gases in the atmosphere: It takes in carbon dioxide (CO_2) gas and produces mevalonate, a useful building block for pharmaceuticals.

The increasing concentration of greenhouse gases in the atmosphere has led to widespread global warming. To begin to address the problem, greenhouse gas emissions, including CO_2, need to be significantly reduced. On top of that, the CO_2 already present could be removed.

Methods to capture CO_2 are in development, and one promising option involves microbes. Genetic engineering can modify their natural biosynthetic pathways, turning the microbes into miniature living factories that can produce all sorts of things—for example, insulin.

One potential microbial factory is Cupriavidus necator H16, a bacterium favored thanks to its relatively unfussy nature about what it's fed. Because it can survive on little more than CO_2 and hydrogen gas, the bacterium is a great candidate for capturing and converting the gases into larger molecules. But even though the microbe's DNA can be rewired to produce interesting products, it's not great at remembering those new instructions over time.

To put it scientifically, the plasmids (the genetic instructions) are relatively unstable. Katalin Kovacs and colleagues wanted to see if they could improve C. necator's ability to remember its new instructions and produce useful carbon-based building blocks out of CO_2 gas.

The team got to work hacking C. necator's biochemical pathways responsible for converting CO_2 into larger six-carbon molecules. The key to improving the plasmid's stability lies in an enzyme called

RubisCo, which allows the bacterium to utilize CO_2.

Essentially, the new plasmid was paired to the enzyme, so if a cell failed to remember the new instructions, it would fail to remember how to make RubisCo and die. Meanwhile, the remaining cells with better memories would survive and replicate, passing along the plasmid.

In tests, the newly engineered microbes produced significantly more of the six-carbon molecule mevalonate compared with a control strain. Mevalonate is a molecular building block for all sorts of substances in living and synthetic systems alike, including cholesterol and other steroid molecules with pharmaceutical applications. In fact, this research produced the largest amounts to date of mevalonate from CO_2 or other single-carbon reactants using microbes.

The researchers say this is a more economically feasible carbon fixation system than previous systems involving C. necator, and it could be expanded to other microbial strains as well.

More information: Marco Garavaglia et al, Stable Platform for Mevalonate Bioproduction from CO_2, *ACS Sustainable Chemistry & Engineering* (2024). DOI: 10.1021/acssuschemeng.4c03561

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