A synthetic biological metabolic pathway fixes CO2 more efficiently than plants

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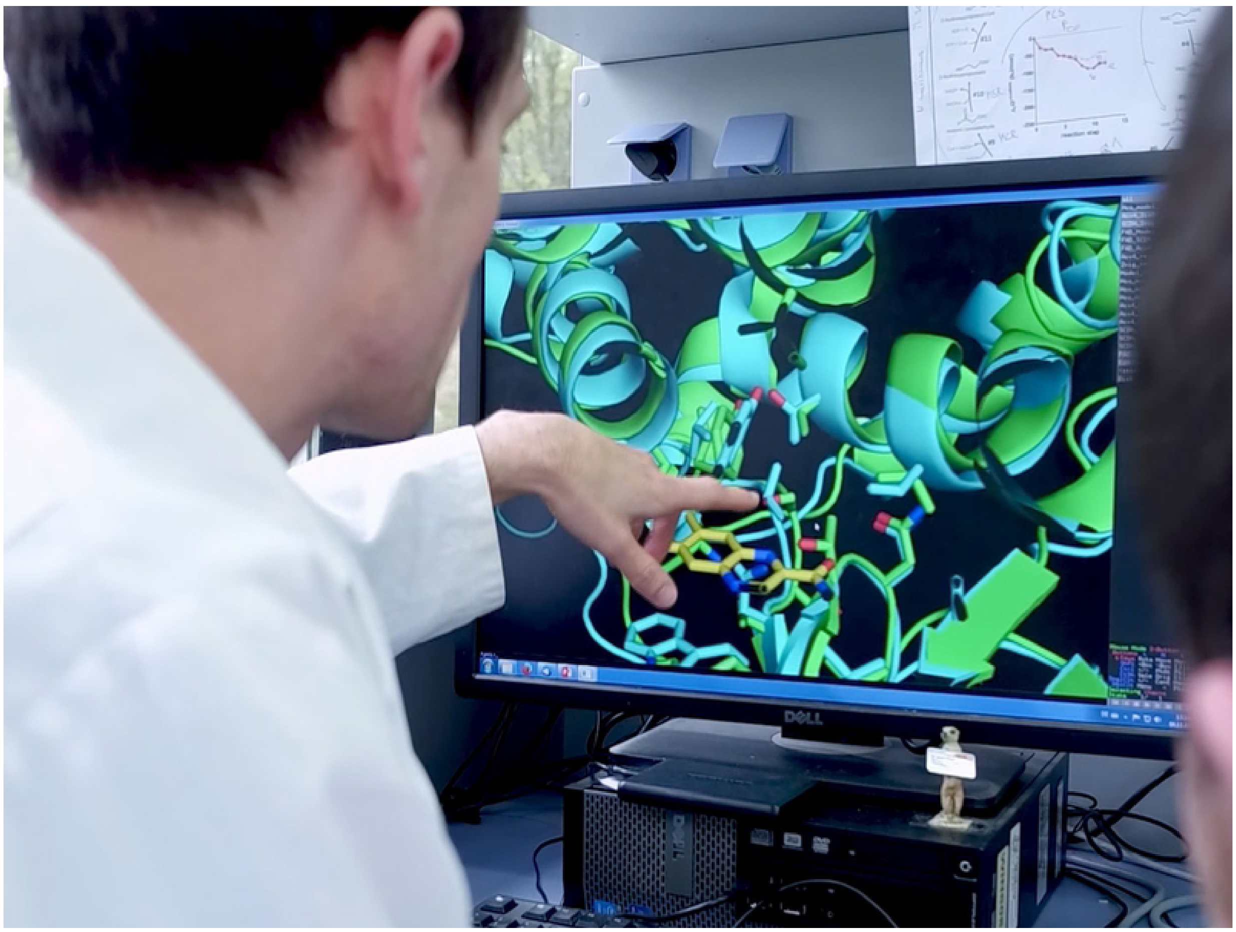

Researchers at the Max Planck Institute for Terrestrial Microbiology have tailored some enzymes – including through the use of computer simulation – to make them compatible with the CETCH cycle. This synthetic metabolic pathway fixes CO2 from the atmosphere much more efficiently than the Calvin cycle in plants. Credit: mediomix / MPI for Terrestrial Microbiology

In future, greenhouse gas carbon dioxide could be removed from the atmosphere by deploying a new biological method. A team headed by Tobias Erb, Leader of a Research Group at the Max Planck Institute for Terrestrial Microbiology in Marburg, has developed a synthetic but completely biological metabolic pathway based on the model of photosynthesis that fixes carbon dioxide from the atmosphere 20% more efficiently that plants can photosynthetically. The researchers initially planned the new system, which they presented in the magazine *Science* this week, on the drawing board and then turned it into reality in the laboratory.

Climate change is one of the most pressing challenges of our time. The concentration of carbon dioxide (CO2) in the atmosphere owing to human activities has continually risen since the start of the Industrial Revolution. All scientific evidence indicates that this increase is exacerbating the greenhouse effect and changing the climate. The consequences are already clearly evident. To overcome the environmental as well as the social challenge of climate change, "we must find new ways of sustainably removing excessive CO2 from the atmosphere and turning it into something useful," underlined Erb, who leads a Junior Research Group at the Max Planck Institute in Marburg.

Theoretically, the problem could be tackled through greater productivity in agriculture and forestry. This is because plants fix carbon dioxide from the atmosphere through photosynthesis. They produce sugar for food from the CO2 via a gradual process known as the Calvin cycle. Each individual biochemical step towards producing the sugar is initiated or accelerated by its own enzyme. The various biocatalysts are precisely aligned with one another to ensure they can work together. However, there is a problem. The CO2-fixing enzyme in the Calvin cycle in plants, which is known by experts as RuBisCo, is relatively slow. It also frequently makes mistakes. RuBisCo captures an oxygen molecule instead of CO2 in one in five reactions.

A bacterial enzyme fixes CO_2 accurately and at high speed

"CO_2-fixing enzymes of a completely different quality are found in nature," emphasized Erb. Such enzymes, which are faster and more efficient than RuBisCo in plants, work naturally in the metabolism of microorganisms. Erb himself succeeded in isolating one of these enzymes – with the unpronounceable name of "Crotonyl-CoA Carboxylase/Reductase" – from bacteria. This enzyme almost never makes mistakes and is also turbo-charged, so to speak, working at twenty times the speed of its counterpart in the plant world.

While at the Federal Institute of Technology Zurich, Erb and his team began exploring how the turbo-enzyme could be deployed to convert CO_2 into organic carbon compounds. This requires additional enzymes as in the Calvin cycle. However, the researchers were unable to simply transfer them from the Calvin cycle because their biocatalysts were not compatible with the turbo enzyme.

A metabolic pathway with 17 enzymes from nine organisms

Tobias Erb therefore initially designed a new theoretical cycle known as CETCH – which stands for Crotonyl-CoA/Ethylmalonyl-CoA/Hydroxybutyryl-CoA – with potential matching enzymes and all biochemical reactions. From databases containing 40,000 known enzymes, he identified a few dozen candidates which could perform the required tasks.

Erb's team then combined all the enzymes in a test tube to produce an "optimized cycle that performed robustly" in just two years. The researchers continually tested new biocatalysts, which were often genetically modified, and tried out new combinations of enzymes to find the system in which the components performed optimally together.

The end result was a synthetic CO2-fixing cycle, something which, as far as Erb is aware, "nobody has ever achieved before." A total of 17 different enzymes, including three "designer enzymes", are used from nine distinct organisms including human beings. The bottom line is that the CETCH cycle, where the Marburg-based researchers emulate photosynthesis's dark reaction, fixes CO2 at 20% greater efficiency than the Calvin cycle in plants.

The CETCH cycle can produce various substances

The synthetic metabolic pathway of the Max Planck team in Marburg therefore represents a pioneering achievement in the field of synthetic biology. The scientists hope to use it to create new systems and organisms beneficial to humans based on biological principles.

The energy in Erb's model cycle currently comes from a chemical reaction and not from light as with photosynthesis in plants and it ultimately produces glyoxylic acids. "However, the CETCH cycle can be modified to produce raw materials for biodiesel, for example," explained the Marburg-based researcher, or indeed antibiotics and many other substances.

Application in bacteria, algae or in combination with solar cells

The genes required for the cycle could be transferred to bacteria or algae for practical application. These modified microorganisms would then produce the product required and could simply use the CO2 from the atmosphere to do so. They would be converting the atmospheric greenhouse gas in a beneficial way. However, the CETCH cycle could also be coupled with solar cells and the electrons that they provide could be used to convert CO2 into useful chemical compounds.

Such visions no longer appear beyond the realms of technical feasibility. Intensive research is currently being conducted by the Max Planck Society's MaxSynBio network on acquiring knowledge on how new biological processes can be created from scratch. Tobias Erb hopes to play a part in helping to understand the fundamental construction principles of metabolism. "Our research aims to reinvent the conversion of inanimate CO2 into organic matter. Our dream is to create a synthetic metabolism 2.0 by using tailored enzymes which can produce any CO2 compound."

More information: A synthetic pathway for the fixation of carbon dioxide in vitro. *Science*, 18 November 2016; DOI: 10.1126/science aah5237

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