Biologist discusses a synthetic metabolic pathway that fixes carbon dioxide and synthetic biology

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Tobias Erb, Leader of the Research Group Biochemistry and Synthetic Biology of Microbial Metabolism. Credit: © MPI for Terrestrial Microbiology

A synthetic metabolic pathway developed by Tobias Erb and his colleagues at the Max Planck Institute for Terrestrial Microbiology in Marburg converts CO2 from the atmosphere into organic matter more efficiently than plants are able to through photosynthesis. We asked the researcher what significance this process could have for climate protection, discussed the hurdles the research team had to overcome to achieve their goal, and looked at the new perspectives that synthetic biology opens up.

Does the synthetic metabolic pathway that fixes CO2 now represent an effective means of curbing climate change?

Firstly, we are aiming to understand the fundamental biological and chemical principles of how CO2 in gaseous form can be converted into organic molecules. Our primary motivation is not stopping climate change. We are seeking to develop atmospheric CO2 as a source of carbon for the future using biological methods. Producing a CO2-neutral process or even one that removes CO2 from the atmosphere and has a positive impact on the climate would be a fantastic secondary effect.

I nevertheless believe there are many ways of stopping climate change. The simplest starts with saving energy every day. I also think we can utilize and improve the biology of CO2 fixation. Designer metabolic pathways, which consume less energy per CO2 molecule converted or fix CO2 from the atmosphere more quickly, obviously represent an interesting approach for producing CO2-based biotechnology.

How close to application are you with the process at the moment?

Our work is primarily still pure basic research. We succeeded in newly creating a fundamental process of life – the conversion of CO_2 into organic matter – in a test tube for the first time ever. We effectively produced a metabolic organ in the test tube. However, transplanting this metabolic organ into living organisms represents a completely different challenge.

Why does transplantation to living cells present such a challenge?

We are unable to predict how our cycle, consisting of 17 reactions, will behave in a cell where 3,000 different reactions are taking place simultaneously. A successful transplantation will clearly take a great deal of time. The Max Planck Society is providing me and my Group with the opportunity to focus on this next, complex step but the outcome is far from certain. Although our calculations essentially indicate that our new path could perform in a more energy-efficient way than natural metabolic pathways in plants, we would have to prove this in experiments.

What were the most difficult aspects of developing the synthetic metabolic pathway?

The greatest difficulty was not devising the metabolic pathway on the drawing board – that only took a week or two. But we then spent over two years on implementing the theoretical cycle in experiments. First of all, we had to find all the individual biological components of the cycle, the enzymes, and bring them together. We had to identify a handful of potential candidates out of over 50 million known genes and 40,000 enzymes and to test them individually and in interaction with other components.

Were there any obstacles you were initially unable to

progress past?

We were unable to get the cycle working at all for a long period. The problem was that an enzyme initially only worked with a chemical agent – a ferrous compound to be precise – which made other enzymes flocculate, thus removing them from the solution. We firstly had to convert this enzyme to use it as an oxygen agent that was compatible with other partners.

What other problems did you encounter along the way?

A second major obstacle was that the cycle only worked slowly in the beginning and quickly faltered. This was due to too many reaction errors. We eventually found what at first glance seemed an unconventional solution. We simply added more enzymes to the cycle. The task of these additional enzymes was just to correct the reaction errors within the cycle. As biologists, we have clearly paid far too little attention to these metabolic corrective loops but they also appear to be very important in natural metabolism.

The synthetic approach is still relatively new in biology. How does this approach differ from that in other biological disciplines?

This synthetic method still remains unusual for us as biologists. We are used to taking biological systems apart and analysing them but not constructing new ones from scratch. We had to find our way slowly and in several stages because we had hardly any rules for the design of synthetic systems beforehand. For example, we firstly have to find out which enzymes are compatible and what factors we need to take into account when creating a complex biological system. Nature may separate cellular processes in the mitochondria, ribosomes and other organelles because they have to take place in different environments and are incompatible with one another. We still have to establish when the best time is exactly to separate biochemical reactions from one another.

Synthetic biology is often criticized for seeking to create artificial life. But doesn't your work also show that it is not usually about that?

We do not wish to play at being God. Creating an artificial, living cell is still a long way off in my opinion. Firstly learning to re-programme individual living processes is a more realistic objective, which is what we are attempting to do at the Max Planck Society's MaxSynBio network. It would be fantastic, for example, if we were able to develop a biological production cycle that repairs and sustains itself. Biological systems often work much more efficiently and under milder conditions than purely chemical ones. By seeking to recreate such systems, we come up with new ideas because we see a lot of enzymes at work.

In which areas could synthetic biology be particularly useful?

I don't think we can even estimate the true potential of synthetic biology. In this respect, we should perhaps take a lead from chemistry which gradually developed from being an analytical to a synthetic discipline over the course of the 19th century. This transformation paved the way for completely new materials and medicines. I'm certain that synthetic biology can achieve similar feats but such development takes time and we must firstly understand the fundamental principles of how to construct complex biological systems.

What major obstacles still have to be overcome?

Biological systems are generally highly complex and heavily interconnected, which makes replicating them and constructing new ones very difficult. An enzyme is not just a biocatalyst that facilitates a chemical reaction, but is also directly linked to its chemical products because the product controls the enzyme. As soon as enough of a substance has been produced, it obstructs the catalyst. In this respect, function and exchange of information are often closely interlinked in biological systems.

Do biological systems have other particular traits?

Biological systems differ from technical systems, as they are capable of adapting and developing. However, this also means that biological systems are not perfect. It is only because enzymes make errors and catalyse secondary reactions that they have the opportunity to develop new functions. It is a bit like taking the wrong turn on your bicycle one time and discovering a shortcut home. In exactly the same way, enzymes also develop new, improved routes by making mistakes.

To make biology synthetic, we therefore have to understand how to integrate imperfection, evolution and complexity into the structure of biological systems. Much more basic research is required to understand the fundamental rules.

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