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NOTES & THEORIES

DISPATCHES FROM THE SCIENCE DESK



Harvard scientists to make LSD factory from microbes

Simple microbes such as those found in baker's yeast can be modified to make LSD, suggests research by Harvard scientists



Students on a bread making course. But did the tutor remember to warn them about the other things that yeast turn into? Photograph: Fabio De Paola

Jake Wintermute wanted to save the world rather than make a pile of money. A PhD student in Pam Silver's synthetic biology lab at Harvard Medical School he worked on biofuels in the hope of one day making them commercial alternatives to fossil fuels.

From time to time, venture capitalists would come by for a chat. They were hard-nosed business types who had an eye on the bottom line and some tough advice to share. They said developing biofuels was a terrible business strategy, because fuel was so cheap. Why not make expensive compounds, like pharmaceuticals, instead?

The advice got Wintermute thinking. What was the most valuable compound they could make with the toolkit of synthetic biology? Some research came up with a few candidates including a few very sophisticated cancer drugs. But another compound was up there in monetary terms: LSD. The value by weight was astronomical.

Wintermute and his colleagues had a good laugh about that. But the more they looked into it, the more interesting - and viable - the drug looked. Around 20 tonnes of lysergic acid, a precursor of LSD, are made each year and turned into real medicines, such as nicergoline, a treatment for dementia. The drug is purified from big vats of fungus (which make the compound naturally) using technology developed decades ago.

With the tools of synthetic biology, Wintermute thought they might do better. The

ergot fungus takes lysergic acid and turns it into a huge variety of exotic molecules. They could mix and match biological pathways from different species of ergot fungus and make potentially new drug molecules. They might even come up with a next generation dementia drug.

Wintermute gave an update on the project last week at the Synthetic Biology 5 conference at Stanford University. As yet he is not making any lysergic acid, but he has dropped two of the six required biological pathways into baker's yeast, which merrily churns out intermediate compounds. At a rough estimate, he expects a litre of modified yeast in broth will produce a gram of lysergic acid. Once made inside the yeast, the drug should pass through the cell walls, where it can be separated out and purified.

This could be the first step towards a new living factory for making LSD, and thanks to previous experience with microbes, scaling up this kind of technology should not be too arduous for the pharmaceutical industry. The work brings to mind a more developed effort by Jay Keasling and others to engineer microbes to churn out useful biofuel components.

Wintermute's work was just one project that got some attention at the SynBio5 conference. Another line of work that caught my eye addressed one of the main concerns over synthetic biology, which is unintended release and potential harm caused by engineered organisms. One way to do this is to make organisms that use genetic material that differs from DNA and RNA. Do this and you can make what people like Markus Schmidt at the Organisation for International Dialogue and Conflict Management in Austria, call "orthogonal life", or organisms that are isolated from the natural environment by virtue of what amounts to a genetic firewall. How well it might work is so far unknown.

An intriguing point raised by Wintermute is that as synthetic biology procedures get cheaper, it will become inevitable for people to replicate and share stuff for free. Once upon a time we used to worry about - or take advantage of - online file sharing. Will the sharing of biological materials bring problems of its own?

These are early days for synthetic biology, but conferences like SynBio5 give us a glimpse of the potential this technology has. One announcement at the meeting came from DARPA, the pentagon funding body that backs high-risk research, in which the agency declared they are getting into synthetic biology in a big way. The ball will soon be rolling. Next week, DARPA is holding a Living Foundries industry day, where synthetic biologists can pitch their big ideas.

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