Synthetic biology for natural products

A summary of a public panel discussion considering perspectives from academia, policy, public and industry

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"A world where plantations and chemical industries are replaced by fermenters?"

Since the industrial revolution there has been an ongoing shift in the way, we produce drugs, chemicals, dyes, and micronutrients. These compounds used to be isolated from cultivated plants using chemical extraction methods. This process has been supplanted by *de novo* synthesis through synthetic chemistry and more recently by synthetic biology.

New advances in synthetic biology have discovered ways to replace the cultivation of, for example, the anti-malarial drug plant artemisia, poppy and vanilla with yeast fermentation, a process akin to "brewing beer". These advances often lower the price of the products and can lead to widespread adoption of life-saving drugs. However, they may also pit large multinational companies against the interests of smallholder farmers in the developing world producing natural-based products. Further, while some of these products are marketed as natural (since they are produced through biological and not chemical means), others feel that this is an attempt to deceive consumers. Our discussion covered several of these aspects and we were even able to come up with a couple of ideas to tackle these thorny issues.

Our panel comprised of representatives from academia (Prof. Hervé Vanderschuren, University of Liège; Dr. Ana Deplazes-Zemp, University of Zurich), the policy world (Dr. Karin Metzlaff, European Plant Science Organisation), public interest organisation (François Meienberg, PublicEye)

and industry (Dr. Brian King, TychoBio). The entire 90-minute discussion is available for public viewing at https://youtu.be/oWGR4bp9avQ.

i. Technology

Brian King began the discussion by introducing the technology of synthetic biology for natural product synthesis. He described how, through genetic engineering, scientists can move plant metabolic pathways into easier to grow organisms like yeast to more efficiently produce plant compounds like vanilla etc. He also talked about how scientists can now combine metabolic enzymes from different species or to engineer completely new enzymes, all of which can help with more efficient production of natural compounds. Most of the panel agreed that this was a positive development, which could accelerate the production of important chemicals and pharmaceuticals and lead to new breakthroughs. However, Ana Deplazes-Zemp pointed out a real biosafety concern with certain instances of this technology. She argued that the recent publication of the production of opiates in yeast (Galanie et al 2015) could lead to misuse and potentially make the production of illicit drugs easier.

ii. Access and benefit sharing

Our discussion took place only a couple of days prior to the 2016 Conference of Parties for the Cartagena and Nagoya protocols and hence a sizeable fraction of the discussion focused on access and benefit sharing (ABS). François Meienberg first raised this issue pointing out that in several instances the knowledge of indigenous peoples in the Global South has been exploited by large companies with no compensation. Overall, the panel was welcoming of the idea that synthetic biology companies should participate in ABS. Hervé Vanderschuren, however, pointed out that the Nagoya protocol could result in South-South discord by citing the example of cassava. Cassava is originally a South American crop, which is now majorly produced in Africa. Breeders in Africa have expressed concern to Hervé that ABS protocols might impede breeding activities for example between South-South countries.

Interestingly, Karin came up with a novel alternative to the Nagoya method of access and benefit sharing. She proposed a solution where companies engaged in sequence data mining would pay a fee for using this data to a

global fund rather than to individual nations. While addressing the concerns to Nagoya raised by Hervé, this would still meet the requirements supported by François Meienberg. In a positive development, both François Meienberg and Brian King agreed that such a solution seemed feasible to them.

iii. Labeling

Apart from these two major issues, we also discussed labelling of natural products made using synthetic biology and whether there is a conflict between the need for transparency and misinformation (please check out the video for the full discussion).

The panel discussion took place at the Zurich-Basel Plant Science Center (PSC) Symposium "Plants for Health - from research to application" on December 1st, 2016. We found the fact that our panellists were able to come to a consensus on an alternative to the current Nagoya ABS method particularly refreshing at a time when people with diverging viewpoints seem to simply talk past each other. We think the panel discussion, in general, the idea of debating and discussing the policy implications of the work we do in the lab was well received by fellow PSC members and we hope future symposia will continue to include a science and policy session.