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New anti-malarial ‘biobricks' could pave way for easier, cost-effective production of artemisinin drug

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The biobricks, created via synthetic biology, could one day provide a cheaper means of making the key drug artemisinin

Students from Trinity College Dublin have successfully created anti-malarial ‘biobricks', which could pave the way for easier and more cost-effective production of the key drug *artemisinin*.

The students recently secured a gold medal for their entry in the International Genetically Engineered Machine (iGEM) competition, which challenged them to create a novel product with important real-world applications by using synthetic biology approaches.

Biobricks are essentially DNA fragments that have been modularised and conformed to assembly standards, which means they can be easily integrated in new biological systems. The Trinity team investigated the re-engineering of artemisinin production in *E-coli* to provide a cheaper option with which to fight malaria.

Artemisinin was first identified by the Chinese scientist Tu Youyou, who recently shared the 2015 Nobel Prize in Physiology or Medicine with Trinity alumnus William Campbell and Satoshi Omura, who discovered a therapy to treat roundworm parasite infections.

The majority of artemisinin currently comes from plant extraction and, more recently, from production in yeast cells. However, production costs vary greatly and many sufferers cannot afford the drug, which provided the Trinity team with its key motivation to explore their alternative synthesis pathway.

Undergraduate student in Trinity's school of Biochemistry and Immunology and team leader, Ben Wilson, said:

> We are delighted by the success of the project. Although we have not yet developed a way of producing sufficient quantities of DHAA (dihydroartemisinic acid), the active element of the drug, we have shown that using plant enzymes could help us clear a hurdle previously in the way. Basically, our initial results look very promising. We intend to continue this work in the future, as well as driving further interest and development in Trinity for the growing field of synthetic biology.

Malaria is caused by the parasite, *Plasmodium*, and is transmitted in the bites of *Anopheles* mosquitoes that have picked up the parasite from other recently infected animals they have fed on. When left untreated, it can be fatal, disrupting proper blood flow and impeding the functions of vital organs in the body. The disease claims over half a million lives a year, most of which are children under the age of five, living in Africa.

The team, made up of seven undergraduate and two graduate students from scientific backgrounds, worked through the summer before attending the World Championship in Boston last month. They presented their findings, along with around 300 other teams from universities dotted around the globe.

Professor of Neurogenetics at Trinity College Dublin, Mani Ramaswami, provided insight, guidance and lab space over the summer.

He said:

> The iGEM team was an enthusiastic and innovative group that worked very hard to address biochemical steps that currently limit the production of artemisinin in bacterial cells. In designing their approach, they sought and received crucial advice and assistance from Zagaya and Amyris Inc in California, which are non-profit companies whose landmark research enabled the production of artemisinin in yeast.
>
> *E.coli* cells are unable to proceed beyond a key step in artemisinin synthesis but the iGEM team showed that expression of specific plant enzymes could drive the next step necessary for artemisinin production. It is not yet clear if this enzymatic step works with the efficiency necessary for practical use but the results represent a very impressive effort, which was motivated both by the science and

by the importance of the cause they were addressing.

Professor Ramaswami added:

> Going forward, Trinity needs a mechanism to support regular participation of undergraduate students in the iGEM competition as it provides a rare and visible opportunity for our students to engage in bottom-up innovation.

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