Source: *The Straits Times,* pB15
Date: 9 June 2017

A NEW FRONTIER IN SCIENCE

Synthetic biology is the design and building of biological systems to improve existing functions or introduce new purposes. It draws inspiration from nature and uses materials offered by the living environment. Scientists at the Singapore Consortium for Synthetic Biology and NUS Synthetic Biology for Clinical and Technological Innovation programme tell The Straits Times about some of the exciting work they are doing in the field.

Engineering 'good' bacteria to kill bad ones

We are never alone.

Our bodies are in constant cohabitation with microbial cells. The composition of these microbial cells, an ecosystem known as the microbiome, exerts tremendous influence on our health. Just the right mix of bacteria can help to protect us from numerous chronic and acute diseases.

Recent scientific studies have highlighted the association of the microbiome with medical conditions such as obesity, infections and even depression, and have led to novel therapies. Infection by the bacterium *Clostridium difficile* that causes diarrhoea and more serious intestinal conditions such as colitis, for instance, can be treated by transferring the gut microbiome of a healthy person to a sick patient.

Our research team is working towards identifying the precise "good" bacteria, or probiotics, that can be used to restore function and balance in metabolic diseases such as diabetes and obesity, two pressing health concerns in Singapore.

In addition, we have developed "smart" bacteria that can deliver and release therapeutic compounds where and when they are needed in the body.

For example, we demonstrated for the first time that engineered probiotic E. coli bacteria can sense and eliminate disease-causing bacteria called *Pseudomonas aeruginosa* in the gut of animals.

These Pseudomonas bacteria are multidrug-resistant pathogens and are a major cause of hospital-acquired infections. When tested, the engineered E. coli bacteria were effective at clearing an established Pseudomonas infection in the gut of infected mice.

The next step is to test the engineered seek-and-kill system in humans as a next-generation antibiotic strategy that will precisely target pathogens, while minimising the damaging effect on the gut microbiota that occurs when broad-spectrum antibiotics are used. Such treatments may be very useful for reducing the incidence of multidrug-resistant bacterial infections, which represent an enormous healthcare challenge.

Associate Professor Matthew Chang, Department of Biochemistry, NUS Yong Loo Lin School of Medicine

NOVEL IDEAS

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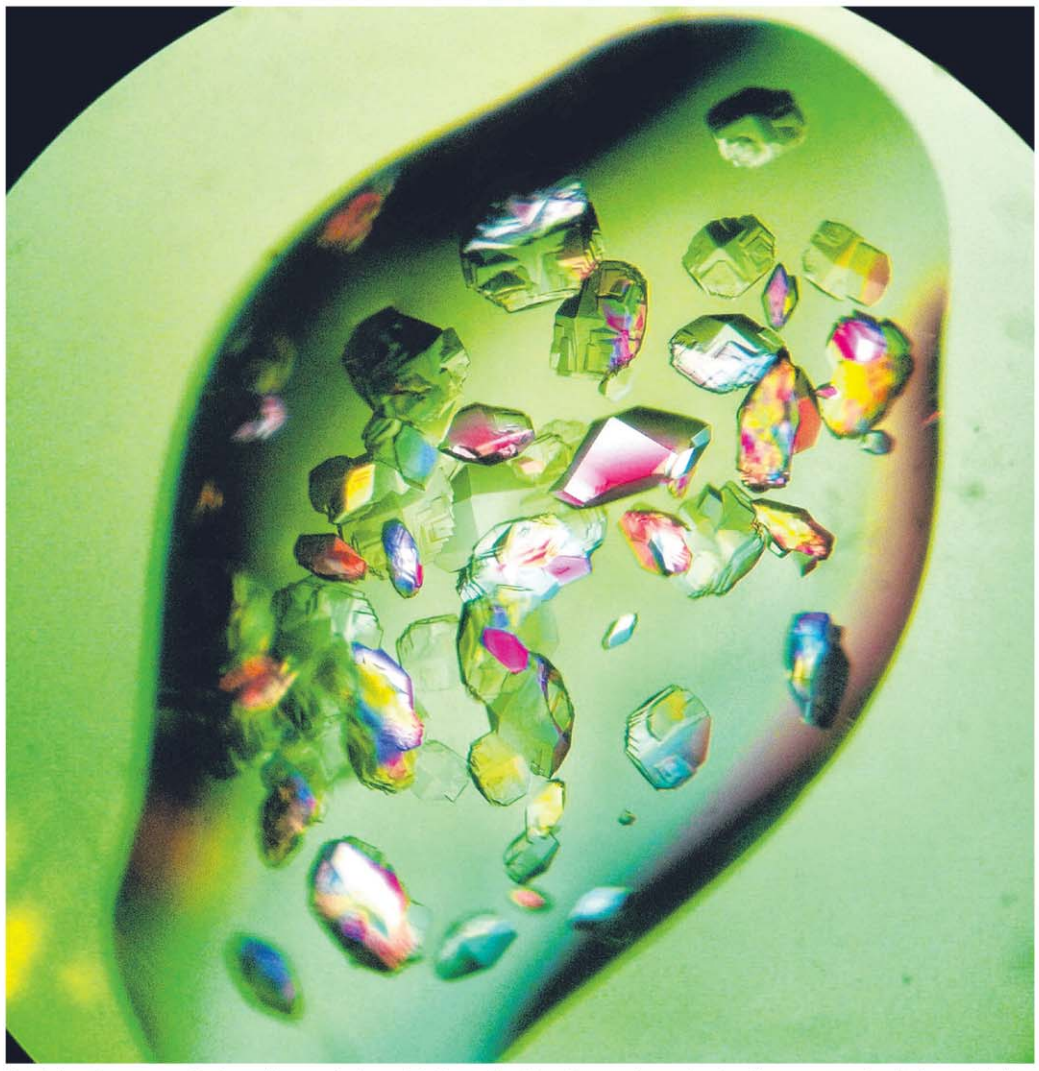
ASSOCIATE PROFESSOR MATTHEW CHANG



Crystals of enzymes that produce caloric restriction mimetics. Researchers aim to discover novel caloric restriction mimetics that are more effective than resveratrol in extending life. PHOTO: NUS

Synthetic biology and the fountain of youth

You can delay the effects of ageing by restricting your caloric intake by 30 to 40 per cent. But who wants to do that?

The key, then, could be to develop a caloric restriction "mimic" that can directly target metabolic pathways affected by caloric restriction. Taking the substance (such as in the form of a pill) would mimic the substantial anti-ageing effects of calorie restriction, without the need to diet or eat less. A present-day example of a caloric restriction mimetic is resveratrol, a substance found naturally in grapes and red wine. Unfortunately, resveratrol is rapidly metabolised in humans and cannot be taken in amounts that would be effective in extending life span without causing toxicity.

Our research aims to discover novel caloric restriction mimetics (mimetics are substances that copy the effects of naturally occurring compounds in bringing about a desired outcome) that are more effective than resveratrol in extending life. By rewiring the metabolic pathways of certain probiotics, such as *Lactobacillus* (found in probiotic drinks), we aim to produce caloric restriction mimetics in probiotics so that we can deliver the benefits of caloric restriction – minus the adverse effects associated with dieting.

Although research is currently at the developmental stage, we have uncovered early promising leads.

We hope that our research can contribute to humanity by providing a modern-day "Fountain of Youth".

Associate Professor Yew Wen Shan, Department of Biochemistry, NUS Yong Loo Lin School of Medicine

Biosensors to cheaply detect infectious diseases

Infectious diseases pose global health challenges.

Cholera, an infectious disease caused by the waterborne *Vibrio cholerae* bacterium, remains a major problem in developing countries. *V. cholerae* is also becoming increasingly antibiotic resistant.

There is a critical need to rapidly detect and identify the bacterium so as to administer the appropriate treatment. The current detection method is still slow or costly.

We are making use of the way *V. cholerae* communicates to develop novel biosensors, and our research team has engineered E. coli to do so.

We are currently developing the sensor into a potentially cheap and easy-to-use diagnostic tool for use in affected areas, moving the technology from bench to bedside.

Using the current system as a blueprint, we are modifying it to detect other superbugs. In the longer term, we envision having a probiotic sensor which can be easily taken in the form of probiotic drinks.

These could then continuously monitor infectious disease-causing bacteria in our gut and produce early warning when bad bacteria are present.

Associate Professor Poh Chueh Loo, Department of Biomedical Engineering, NUS Faculty of Engineering

S'pore hosts global conference

The Synthetic Biology Conference is the world's foremost professional meeting of its kind. Launched in 2004, it brings together a global community of synthetic biology practitioners to share, learn and debate on the latest efforts in the field.

Previous conferences were hosted at leading academic institutions such as the Massachusetts Institute of Technology, Hong Kong University of Science and Technology, Stanford University and Imperial College London.

About 800 participants are expected at this year's conference in Singapore, with more than 70 speakers presenting in 12 thematic sessions. The event will allow Singapore's synthetic biology community to forge new cross-border friendships, facilitate international collaborations and build global partnerships.

The conference, to be held from Tuesday to Friday at NUS' University Cultural Centre, is organised by NUS Synthetic Biology for Clinical and Technological Innovation and the non-profit BioBricks Foundation and SynBioBeta, a community devoted to the responsible growth of the synthetic biology field.