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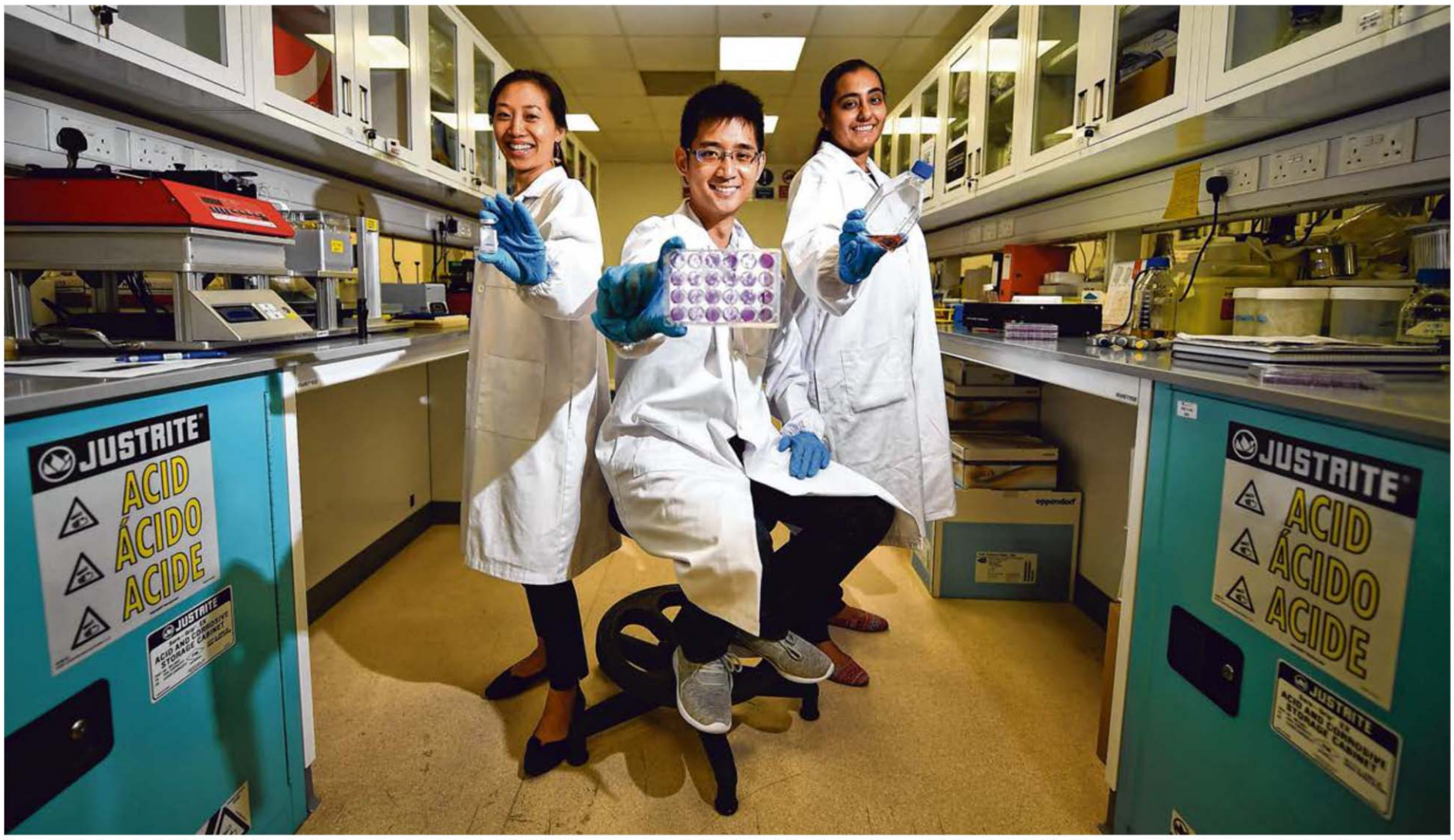

(From left) Principal scientist Debbie Lee with a vial of Tyzivumab, assistant director Chionh Yok Hian with a multi-well plate demonstrating the effectiveness of Tyzivumab against the Zika virus, and laboratory manager Rasvinder Kaur with a flask of cells producing Tyzivumab antibodies. Tyzivumab was fit for clinical trials in just nine months. ST PHOTO: LIM YAOHUI

Shortening the wait for infectious disease cures

Instead of getting antibodies from natural immune response, team engineers one on computer

Samantha Boh

An infectious disease spreads across countries, killing scores of people in months.

Meanwhile, scientists struggle to come up with a cure, hampered by a discovery and development process that takes years.

This narrative is typical during an epidemic.

However, local biotechnology company Tychan might have found a way to shorten the wait for a remedy, having come up with a Zika drug – an antibody it has named Tyzivumab – that was fit for clinical trials in just nine months.

The company is wrapping up phase 1a trials, which it started in February – where the drug was tested for safety and dosage on healthy volunteers – and will be embarking on phase 1b to test the drug on Zika patients.

Professor Ooi Eng Eong of the Duke-NUS Medical School, who founded Tychan with Professor Ram Sasisekharan of the Massachusetts Institute of Technology, said the key lies in the engineering and manufacturing of the antibody.

Antibodies are developed during an infection to kill off the infection-causing antigens, whether they are bacteria, viruses or germs. The antibodies do so by binding onto the antigens in such a way that their functions are inhibited, and also serve to protect the body from subsequent infection.

TARGETED APPROACH

We knew which part of the Zika virus we wanted the antibody to bind to, and so we were able to engineer several candidates on the computer.

PROFESSOR OOI ENG EONG, of the Duke-NUS Medical School.

Traditionally, scientists developing antibodies to combat diseases get them from humans who have recovered from an infection or from animals infected with the virus. This takes months.

However, instead of relying on the natural immune response, the Tychan team designed and engineered the antibody on a computer.

In just two weeks, the team had about 16 potential candidates that they eventually narrowed down to one. Prof Ooi said this was possible because of the team's knowledge of dengue, which is a flavivirus like Zika and behaves similarly.

"The conventional way that scientists do it is to find an antibody that has the ability to inhibit the virus, but they don't know where it binds, Prof Ooi said.

"We knew which part of the Zika virus we wanted the antibody to bind to, and so we were able to engineer several candidates on the computer."

The team targeted a "flap" on the virus protein, engineering antibodies that would sit over it. This prevents the flap from opening to allow the virus' RNA (molecules that carry codes from DNA) genome to get out and into the cells in the body, a step that is essential for virus replication.

The team also managed to streamline the manufacturing process, thanks to advanced sequencing technologies that provide detailed information on the properties of the antibody produced and if they are right.

The project was funded by Temasek Foundation Ecosperity, which has provided close to $16 million worth of funding to 16 projects since its inception in 2016.

Prof Ooi said the technique could be used to speed up the development of drugs for other flaviviruses as well and that the team has started doing so, though he declined to say more.

"But nine months is actually still too long. Our goal is to take this down to weeks," he added.

stnewsdesk@sph.com.sg