

SCIENCE

Zika infections

WARRIORS IN LAB COATS

Researchers in Singapore have joined the war against Zika to create better ways to diagnose, understand and treat the disease and to stop its spread.

Carolyn Khew highlights some of their efforts.

Fogging and the mozzie wipeout aside, local researchers are waging war of a different kind on Zika.

They are trying to unravel the many mysteries of the virus and come up with better ways to diagnose and treat it.

DETECTION

There is already a diagnostic kit developed by Singapore scientists which can test for dengue, chikungunya and Zika all at the same time in just two hours. All that is required from the patient is a blood or urine sample.

Work is also under way to develop other diagnostic tests.

Researchers at the Agency for Science, Technology and Research (A*Star), for instance, are developing tests which can detect whether a person has been infected with the virus even after it is no longer found in the blood. As Zika stays in the bloodstream for only three to four days, this makes it hard to detect if a person is infected after this crucial window period has passed, explained Dr Laurent Renia, executive director of A*Star's Singapore Immunology Network (SIgN).

So a colleague, Dr Lisa Ng, a senior principal investigator at SIgN, together with other researchers from the Bioprocessing Technology Institute (BTI), has been developing new antibody-based tests. (When the body is infected with Zika, the immune system produces antibodies to fight it. This takes about five days to a week.)

Dr Ng's team infected mice with Zika and collected their immune cells. The BTI team then selected a few antibodies out of a few hundred they have identified, which can bind to the virus most effectively. This is important as one of the chal-

lenges in accurate diagnosis is that most antibody-based tests are not specific enough and could mistakenly produce a false positive result. This is because Zika shares similarities with dengue and the rest of the group known as flaviviruses.

Dr Ng's work on Zika started about 1½ years ago, long before the mosquito-borne virus became a concern in Singapore. She wanted to find out the difference between Zika and chikungunya – both of which can cause similar symptoms, such as rashes and joint pain.

"It sparked off the interest and we wanted to develop tools and experimental models to understand immunity against these viruses," she said.

Dr Renia pointed out that the virus was discovered in the 1940s in a Ugandan forest, but almost nothing was known about it before outbreaks in Micronesia in 2007 and French Polynesia in 2013, even though it had spread from Africa to parts of Asia, including India and Malaysia, from the 1960s to 1980s.

"There was only one viral strain available in the publicly available repositories," he said.

"We are constantly monitoring emerging infectious diseases in the region. The symptoms identified in Zika can also be found in dengue and chikungunya. We were thinking it could have caused some confusion and people might have mistaken some Zika cases for dengue and chikungunya."

The number of Zika cases in Brazil has tapered off, after exploding last year. The Washington Post reported in July that the number of cases was down from 3,000 to 3,500 a week earlier in the year to just 30 cases a week in June.

In Singapore, though, the health

authorities last week announced the first case of local transmission. As of Aug 31, the total number of local transmissions stood at 115.

DRUGS AND VACCINES

At Duke-NUS Medical School, structural virologist Lok Shee-Mei is looking at how the Zika virus particles infect cells, and the structural changes behind this. This will suggest sites on the virus which can be targeted by drugs and antibodies, she said.

In April, Associate Professor Lok was among the first in the world to publish a paper detailing an image of the Zika virus in the prestigious science journal *Nature*.

One finding is that Zika is much tougher than the dengue virus. Heating it to 40 deg C failed to kill it, and this explains why it can stay in bodily fluids such as semen and urine, and can be transmitted through sexual contact.

Prof Lok is working on identifying potent antibodies that can prevent Zika infection. This could lead to the development of drugs against the virus. "The use of therapeutic antibodies has been done with other viruses and has proven to be effective."

"There are antibodies that can kill the Zika virus and there are some that may possibly enhance infection. So the key is to find the ones that are very good in killing the virus," she said.

While Zika is considered a generally mild disease, producing symptoms such as rashes and fever which go away in a week, it is closely associated with microcephaly, as a small proportion of infected pregnant women (between 1 and 10 per cent) have given birth to babies with abnormally small heads.

The holy grail would therefore be

to develop drugs or vaccines that can stop it. To that end, Assistant Professor Luo Dahai from Nanyang Technological University's Lee Kong Chian School of Medicine and his colleagues have spent the past year researching the virus.

The expert in the molecular biology of viruses wants to understand the functions of certain Zika proteins. His team compared these proteins with those found in its close cousin, dengue, and discovered some features unique to Zika.

They are now studying a key viral enzyme that is essential for the virus to reproduce itself, making it an ideal drug target. The next step would be to screen for drug-like molecules that can inhibit or stop its function. "Ideally, when these targets are blocked by drugs, they will stop functioning and the virus will stop replicating, thus stopping the infection," Prof Luo said.

MOZZIE CONTROL

While these efforts are in the pipeline, the authorities are not letting up on vector control.

Getting rid of the *Aedes aegypti* mosquito, which carries Zika and dengue viruses, remains crucial.

Besides extended fogging, more checks and reminders to people and companies to keep their premises mosquito-free, the National Environment Agency is starting a field study of some special new mosquitoes. It will deploy male mosquitoes infected with *Wolbachia* bacteria in Braddell Heights, Nee Soon East and Tampines West from next month. Eggs produced when these lab-bred insects mate with their *Wolbachia*-free female counterparts will not hatch, and it is hoped that with this, the mosquito population will fall over time.

Dr Renia said research in Singapore will bring to the table a different understanding of the epidemiology of the Zika virus in this part of the world.

"Compared with Brazil, the United States and Puerto Rico, we are an equatorial country. Humidity and temperature are stable throughout the year," he said.

Moreover, the difference in genetic background between Asian and Caucasian populations could mean the infection may develop differently, and that people might present different disease profiles.

"This will enable us to devise more personalised treatments," he added.

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