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S'pore team closer to creating 4-in-1 'cocktail' to fight dengue

Antibodies now identified for 3 of 4 strains; second team looks at epidemic-prone viruses

Feng Zengkun

Singapore researchers are one step closer to whipping up a "drug cocktail" that can attack all four strains of the dengue virus, and they have also discovered why some dengue strains are more likely to lead to epidemics than others.

The dengue virus has four serotypes, or strains, circulating in nature, which makes it difficult to fight. When a person is infected with one serotype, his body can generate protection against that serotype, but not against the others.

If he is infected later with a different serotype, he has a higher chance of developing more severe and possibly fatal symptoms such as dengue haemorrhagic fever.

To provide complete protection against infection, a vaccine has to create an equally strong antibody response against all four serotypes.

Even the latest clinical trials for one potential vaccine showed mixed results.

They showed good protection against serotypes 3 and 4, poor protection against serotype 1, and no protection at all against serotype 2.

Associate Professor Lok Shee-Mei, who is from the Emerging Infectious Diseases Programme at the Duke-NUS Graduate Medical School, had previously identified antibodies that kill serotypes 1 and 3. In a paper published today in the online edition of prestigious scientific journal Science, Prof Lok and other researchers showed how another antibody could neutralise serotype 2.

The discovery brings the researchers to the brink of devising a drug cocktail that would be made up of four antibodies, each effective against one serotype.

Prof Lok said: "The new human antibody found in this study not only kills the dengue virus serotype 2, but also prevents the development of severe disease stimulated by weaker antibodies.

"This clearly illustrates the potential of using this antibody for dengue treatment."

Separately, another Duke-NUS team led by Associate Professor Ooi Eng Eong identified how small changes in the dengue's genome could allow the virus to penetrate human immune defences and spread more efficiently.

Their paper was also published in today's online edition of Science.

Prof Ooi, who is the deputy director of the infectious diseases programme, said the team had studied a dengue serotype 2 epidemic in Puerto Rico in 1994.

They found that mutations in the tail of the dengue genome enabled it to make short fragments of genomic material consisting exclusively of its tail, which binds to a protein in people and suppresses the human anti-viral response.

This process enabled the new strain to spread more efficiently within an infected person, and increased its chances of infecting new mosquitoes that would transmit the virus.

Prof Ooi said the team had not studied epidemics in Singapore because recent ones here had been the result of alternating dengue serotypes, so the cause could have been low human immunity rather than dengue virus mutations.

"In Puerto Rico, dengue serotype 2 was around all the time, and then suddenly there was an epidemic," Prof Ooi said.

"Our findings show that not all dengue viruses have the same ability to cause epidemics, and they imply that identifying molecular signatures that allow the viruses to spread more efficiently could help focus public health resources on more important strains," Prof Ooi noted.

There have been about 4,200 dengue cases here so far this year.

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Shape-shifting bug harder to kill

Of the four dengue virus serotypes, or strains, serotype 2 is harder to kill because it changes shape when it enters the human body, said Associate Professor Lok Shee-Mei of the Duke-NUS Graduate Medical School yesterday.

Serotypes 1 and 2 are more common in Singapore, and caused recent epidemics here.

Prof Lok said: "A mosquito's body temperature is 28 deg C, and the virus looks very smooth when it is in mosquitoes.

"But the same virus suddenly changes shape when it is in people, who have a body temperature of 37 deg C."

She said some scientists might have been developing vaccines that target the wrong virus structure.

"Most of the dengue virus serotype 2 strains show this kind of change, although there are some that do not," Prof Lok noted.

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