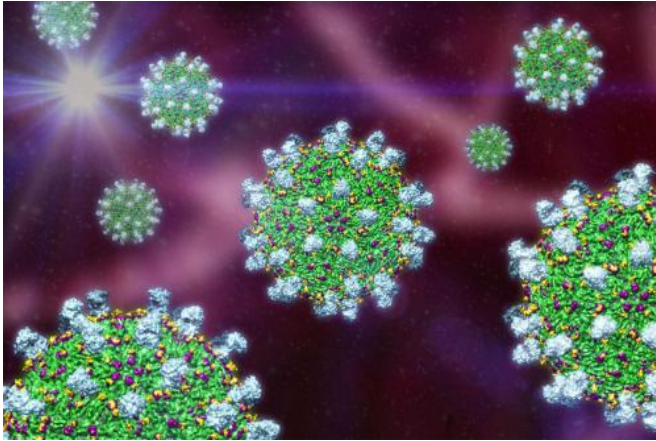


Team finds powerful dengue neutralizing antibody

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Reconstructed visual of dengue virus serotype 3 bound with antigen-binding fragments of super-potent antibody 5J7 Credit: Guntur Fibriansah

A new Duke-NUS-led study has identified a super-potent antibody which requires a minute amount to neutralize the dengue virus.

The study, published online on 20 February 2015, in the journal *Nature Communications*, showed how a newly identified antibody 5J7, is highly effective in killing dengue virus whereby only 10-9 g of antibody is needed to stop the infection of dengue serotype 3 virus (DENV-3). This new finding gives hope for the development of effective dengue treatments.

Over the last 50 years, the incidence of dengue virus has increased by 30 times worldwide. The virus causes fever, rashes and joint pain and in severe cases, bleeding and shock. It is estimated to be endemic in 100 countries and is a huge burden on healthcare systems. However, till now, there is no licensed dengue vaccine or therapeutic agent due to the presence of four circulating virus serotypes (DENV1-4) complicating their development.

Senior author Associate Professor Shee Mei Lok from Duke-NUS Graduate Medical School Singapore (Duke-NUS) focuses her research on understanding the pathology and structure of the dengue virus to develop effective therapeutics. Her lab has already discovered [antibodies](#) that are effective against DENV-1. Her strategy to develop a safe therapeutic is to combine four antibodies that each bind and potentially inhibit infection of each of the dengue virus serotypes.

In this recent study, researchers isolated 5J7 from 200 different candidate antibody molecules by studying blood samples from a dengue infected patient. By examining the virus-antibody complex structure at very high magnification, they showed that each arm of the antibody is surprisingly effective in grabbing three surface proteins on the surface of the virus at the same time. In addition, the sites on the virus where the antibody was bound were critical for the virus to invade cells.

"This kind of binding with the virus has never been observed and it explains why the antibody itself is so highly potent." said A/Prof Lok, who is from the Emerging Infectious Diseases Programme at Duke-NUS. "The movement of virus surface proteins is highly essential for invading cells - you can think of antibody 5J7 locking the virus [surface proteins](#), thus strapping the virus."

While antibody 5J7 has been found to be effective against DENV-3, the remaining two serotypes of [dengue virus](#) (DENV-2 and DENV-4) have to be considered. When a patient is infected by one serotype - this stimulates the production of a variety of antibodies that kills that serotype and that patient will have life-time immunity towards that particular serotype. However, in this process, the patient will also produce antibodies that will bind the other three if they are infected by them. This may enhance their secondary infection and cause the development of a more severe form of the disease.

"We need to test the efficacy in mouse models first and then move to clinical trials," said A/Prof Lok about the next step after this promising finding. "We are optimistic that we will make a treatment breakthrough within these few years but antibodies against all the other serotypes have to be identified first."

Provided by Duke University

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