Human antibody for dengue virus isolated

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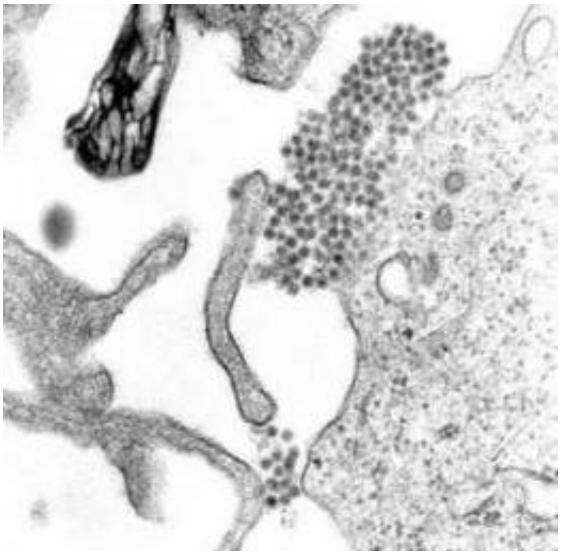

A TEM micrograph showing Dengue virus virions (the cluster of dark dots near the center). Image: CDC

(Phys.org) -- A group of scientists in Singapore and the UK have isolated a human antibody capable of effectively neutralizing the mosquito-borne dengue virus. Dengue fever is currently incurable and infects an estimated 100,000 people a year, mostly in the tropics. The only treatment is alleviating the symptoms, which can include intense joint and muscle pain, nausea, vomiting, high fever, and death in severe cases.

Dengue virus (DENV) has four strains or serotypes (1 to 4), and a person infected by one serotype produces antibodies that make them immune for life to infection from that serotype, but that usually only give limited

or transient immunity to the other three. The newly isolated antibody is extremely effective for serotype 1.

The researchers isolated the human antibody, HM14c10, which was formed in the body of a patient in Singapore who had recovered from a DENV1 infection. The antibody turned out to be extremely fast-acting and gave powerful immunity to the virus.

The group recruited around 100 recovered dengue patients and found over 200,000 antibodies in total. The HM14c10 antibody turned out to be so powerful that it kills the virus before it is able to infect the cells, according to lead researcher, Professor Lok of the National University of Singapore.

After isolating the antibody the researchers carried out experiments on mice and discovered that it functions by stretching across the virus surface, preventing the changes to its surface proteins that must take place for the virus to be able to infect cells.

The paper was published in the journal *Science Translational Medicine*, and the findings may help researchers develop new therapies to treat or prevent infection by the dengue virus. The research showed the antibody to be far more effective at neutralizing viruses than the anti-dengue chemicals now in development.

The next phase of the research on DENV1 will be clinical trials to test the antibody on patients infected with DENV1. The team will also continue to check the remaining antibodies in their library to determine if any are as effective against the other serotypes, and they have already found a likely candidate against serotype 2.

Another lead author of the paper, Dr Paul A. MacAry of the National University of Singapore said that in Singapore around 90% of dengue

fever cases were either DENV1 or 2, and their research should lead to an antibody for each of these strains within about six months.

More information: The Structural Basis for Serotype-Specific Neutralization of Dengue Virus by a Human Antibody, *Sci Transl Med* 20 June 2012:
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ABSTRACT
Dengue virus (DENV) is a mosquito-borne flavivirus that affects 2.5 billion people worldwide. There are four dengue serotypes (DENV1 to DENV4), and infection with one elicits lifelong immunity to that serotype but offers only transient protection against the other serotypes. Identification of the protective determinants of the human antibody response to DENV is a vital requirement for the design and evaluation of future preventative therapies and treatments. Here, we describe the isolation of a neutralizing antibody from a DENV1-infected patient. The human antibody 14c10 (HM14c10) binds specifically to DENV1. HM14c10 neutralizes the virus principally by blocking virus attachment; at higher concentrations, a post-attachment step can also be inhibited. In vivo studies show that the HM14c10 antibody has antiviral activity at picomolar concentrations. A 7 Å resolution cryoelectron microscopy map of Fab fragments of HM14c10 in a complex with DENV1 shows targeting of a discontinuous epitope that spans the adjacent surface of envelope protein dimers. As found previously, a human antibody specific for the related West Nile virus binds to a similar quaternary structure, suggesting that this could be an immunodominant epitope. These findings provide a structural and molecular context for durable, serotype-specific immunity to DENV infection.