Details of monkey antibodies against chikungunya virus could help to fight the disease in humans

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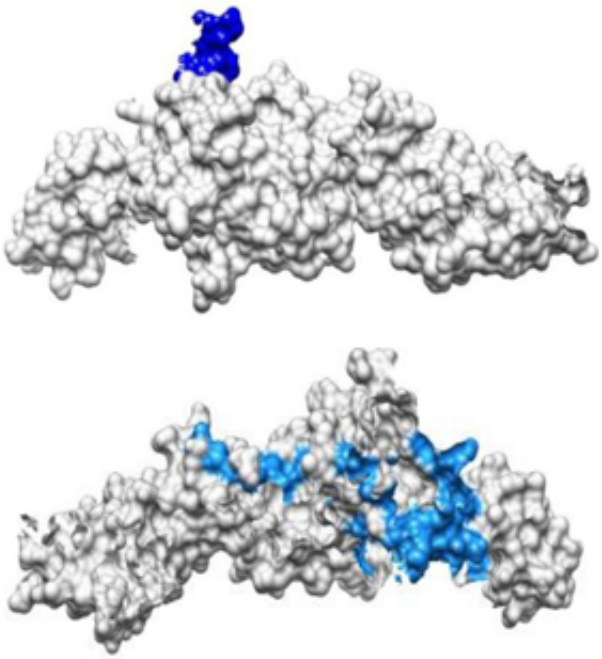

Two views of the chikungunya virus E2 glycoprotein, showing two sites (blue) that both macaque and human antibodies bind. Credit: Y.-W. Kam et al.

Chikungunya fever can cause severe and long-lasting joint pain, with several epidemics affecting multiple continents in the past decade. The illness is caused by chikungunya virus (CHIKV), but there is no effective vaccine or drug against it. Now, research led by Lisa Ng from the A*STAR Singapore Immunology Network provides details of how the

immune system responds to CHIKV—findings that could support the development of vaccines and therapies.

One problem in developing therapies against CHIKV is that most animal studies tell us little about the disease in humans. To address this, a group led by Pierre Roques at the French Alternative Energies and Atomic Energy Commission have developed a model in macaque monkeys, which are biologically very similar to humans. Ng and colleagues conducted experiments using these macaques, in line with European directives for good animal practice.

"Macaques are susceptible to experimental CHIKV infections and serve as an effective non-human primate model for detailed studies," explains Ng. "The close evolutionary relationship between macaques and humans allows researchers to predict the effects of the disease in humans based on observations in macaques."

Ng and her team analyzed antibodies taken from the blood of macaques infected with CHIKV at 16 days and 180 days after infection. They found that the antibodies did not just tag the virus—so that immune cells could recognize and destroy it—but also could disable the virus on their own.

They also identified several specific sites on CHIKV proteins to which the antibodies bound. A number of these sites had not been previously identified, but two of them matched sites that are also recognized by human CHIKV antibodies (see image). Both sites are at one end of a structural CHIKV protein called E2 glycoprotein.

The researchers also looked at how the immune systems of the macaques responded to two different strains of CHIKV with slightly different versions of E2 glycoprotein. Macaques infected with a strain called IMT, isolated from La Reunion Island in the Indian Ocean, had a stronger

antibody response than animals infected with a strain isolated from Singapore called SGP11. Their findings correspond with observations in humans infected with the different CHIKV strains.

"These findings highlight the similarity of anti-CHIKV antibody responses in humans and macaques and also emphasize the importance of E2 glycoprotein in vaccine formulation," says Ng. "Our study provides critical knowledge to improve understanding of CHIKV infection and immunity, vaccine design and preclinical studies."

More information: "Kam, Y.-W., Lee, W. L., Simarmata, D., Le Grand, R., Tolou, H. et al. Unique epitopes recognized by antibodies induced in chikungunya virus-infected non-human primates: Implications for the study of immunopathology and vaccine development." *PLoS ONE* 9, e95647 (2014). dx.doi.org/10.1371/journal.pone.0095647

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