Existing drugs could treat chikungunya

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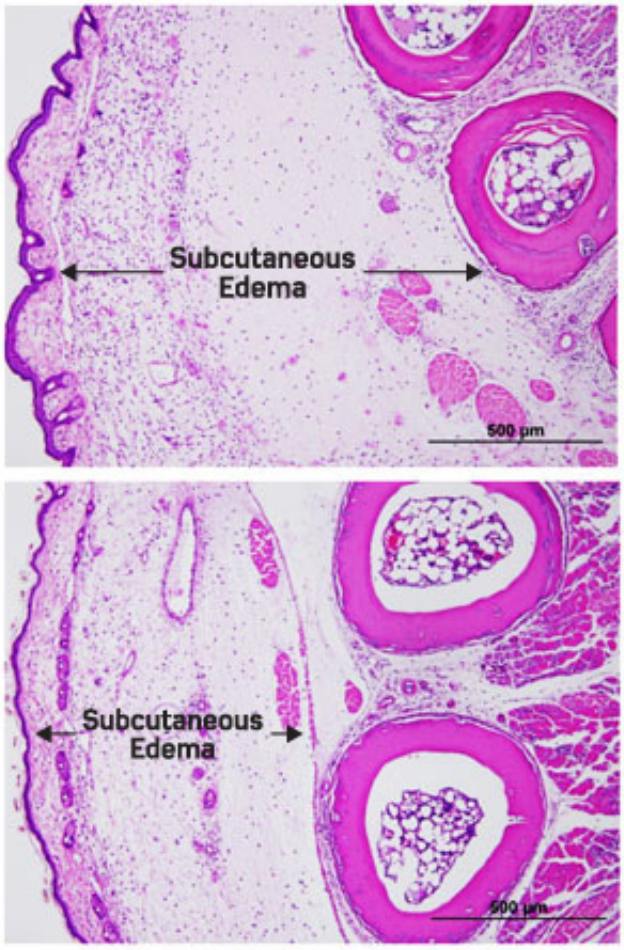

The degree of subcutaneous edema during Chikungunya infection (top) and the fingolimod treated mice (bottom) during the peak of joint swelling. Credit: Ref. 1. © Teo et al., American Association for the Advancement of Science

Chikungunya virus (CHIKV) infection could be treated with

autoimmune therapies currently used for other conditions, according to research led by A*STAR scientists.

When transmitted to humans by mosquitoes, CHIKV causes high fever, headaches, joint inflammation and debilitating joint pain. Since 2004 there have been major outbreaks in Africa, Asia, the Caribbean, and South and Central America. There are currently no approved treatments.

A group led by Lisa F. P. Ng at the A*STAR Singapore Immunology Network (SIgN) demonstrated in 2013 that CD4+ T cells, which mediate immune system responses, play a central role in triggering CHIKV-induced joint swelling.

To investigate, Ng and Laurent Renia, her colleague at SIgN led the team to transfer CD4+ T cells from both healthy and CHIKV-infected mice into T cell receptor-deficient mice. Only those that received cells from infected donors suffered joint swelling, inflammation and skeletal muscle damage—confirming the key role of these T cells in triggering CHIKV symptoms.

They then carried out proteome wide screening assays in which CD4+ T cells taken from CHIKV-infected mice were tested against all proteins generated by the CHIKV virus.

This identified specific segments in two viral proteins, nsP1 and E2, as those that stimulate CD4+ T cell responses to CHIKV. The discovery could be used to help design vaccines against CHIKV and related viruses.

Applying their findings, the researchers treated groups of CHIKV-infected mice with three clinically-approved T cell suppressive drugs. Tissue samples were then visually assessed by histopathologists.

Fingolomid, usually used to prevent multiple sclerosis relapses, successfully reduced joint swelling, inflammation and muscle damage in the rodents. It did so both when given as a prophylactic, and following infection as a standard therapeutic treatment. The other two drugs—cyclosporin A and rapamycin—failed to control the disease symptoms in mice.

Ng and her colleagues stress that the use of fingolomid to treat CHIKV patients with chronic joint pain has yet to be evaluated, but hope their study will lead to further research on whether it and other immunosuppressive drugs could help those with the condition.

"We were pleased with these findings," says Ng. "They demonstrate our previous theory about the pathogenic role of CD4+ T cells was correct, and suggest existing T cell suppressive drugs could provide viable treatment options for patients."

The group believes such drugs could also be used to treat inflammation caused by other arthropod-spread viruses that is mediated by virus-specific CD4+ T cells.

More information: Teck-Hui Teo et al. Fingolimod treatment abrogates chikungunya virus–induced arthralgia, *Science Translational Medicine* (2017). DOI: 10.1126/scitranslmed.aal1333

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