Nature Reviews Rheumatology | Published online 16 Feb 2017; doi:10.1038/nrrheum.2017.21

ACUTE INFLAMMATORY ARTHRITIS

Potential therapies for chikungunya arthritis

Targeting T cells is emerging as a promising strategy for the treatment of chikungunya arthritis. Two independent studies published in *Science Translational Medicine* demonstrated amelioration of disease when targeting pathogenic CD4$^+$ T cells in mice infected with chikungunya virus (CHIKV).

CHIKV disease is a mosquito-borne disease that typically results in arthritic manifestation in the joints of infected patients (chikungunya arthritis) that resembles rheumatoid arthritis (RA). Currently, specific treatments for CHIKV arthritis are lacking. "Previously, we found that CD4$^+$ T cells, and not CD8$^+$ T cells, had a pathogenic role in driving CHIKV-induced joint inflammation," remarks Laurent Rénia, co-corresponding author of the Teo *et al.* study. In this study, the investigators sought to characterize CD4$^+$ T cells involved in CHIKV disease pathogenesis to better understand what processes could be targeted therapeutically.

By use of proteome-wide screening, the researchers identified epitopes within nsP1 and E2 viral proteins that were recognised by splenic CD4$^+$ T cells from CHIKV-infected mice. Transfer of nsP1-specific or E2-specific CD4$^+$ T cells into T cell receptor-deficient mice led to joint inflammation. To explore the effects of T cell modulation on disease pathogenesis, Teo *et al.* tested several clinically approved T-cell-suppressive drugs in CHIKV-infected mice. "Our research shows that fingolimod treatment blocks the movement of CD4$^+$ T cells to the joint of infected hosts, resulting in a reduction of joint swelling," explains Lisa Ng, co-corresponding author on the paper.

> "These therapeutic strategies could also be relevant for the treatment of inflammatory arthritis associated with other infectious diseases"

In a separate study, Miner *et al.* tested eight different DMARDs, which are commonly used to treat patients with RA, in CHIKV-infected mice. "[Previous findings] suggested that DMARD therapies that work in RA and target T cells might also work for CHIKV," says co-corresponding author Deborah Lenschow. Miner *et al.* showed that abatacept (a drug that blocks T cell co-stimulation) and the Janus kinase inhibitor tofacitinib reduced joint swelling in CHIKV-infected mice without increasing viral burden.

Miner and colleagues also found that whereas treatment with either abatacept or an anti-CHIKV human monoclonal antibody partially decreased arthritis severity in infected mice, the combination of these two therapies abrogated the disease phenotypes, as demonstrated by a reduction in joint swelling, chemokine and proinflammatory cytokines levels, and infiltrating leukocytes. "[Our findings] provide a new avenue for possible therapy against CHIKV by repurposing RA-based drugs and combining them with antiviral approaches," states co-corresponding author Michael Diamond.

Together, the results of these two studies show two different T-cell-targeting approaches that ameliorate chikungunya arthritis severity in mice. These therapeutic strategies could also be relevant for the treatment of inflammatory arthritis associated with other infectious diseases. As mouse models do not fully recapitulate human diseases, both groups intend to take these drugs forward to the next stage in drug-testing.

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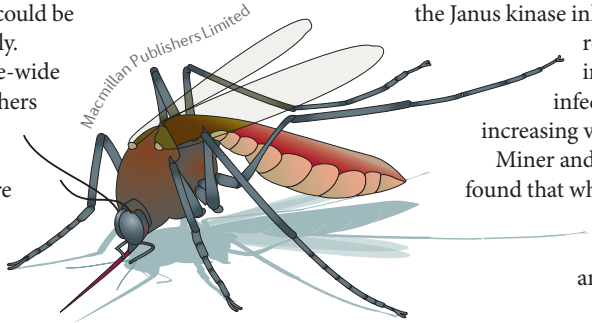

ORIGINAL ARTICLES Teo, T. H. *et al.* Fingolimod treatment abrogates chikungunya virus-induced arthralgia. *Sci. Transl. Med.* http://dx.doi.org/10.1126/scitranslmed.aal1333 (2017) | Miner, J. J. *et al.* Therapy with CTLA4-Ig and an antiviral monoclonal antibody controls chikungunya virus arthritis. *Sci. Transl. Med.* http://dx.doi.org/10.1126/scitranslmed.aah3438 (2017)