Nature Reviews Rheumatology | Published online 1 Feb 2018; doi:10.1038/nrrheum.2018.12

LYME ARTHRITIS

Bystander-activated T cells contribute to Lyme arthritis

The contribution of T cells to the arthritis symptoms that can persist for months or years following antibiotic treatment in patients with Lyme disease are unclear. New evidence from an IL-10-deficient mouse model reveals a role for antigen-independent activation of both $CD4^+$ and $CD8^+$ T cells in the development of Lyme arthritis.

In the study, Sarah Whiteside and colleagues showed that *Il10*$^{-/-}$ mice continue to have arthritis for at least 18 weeks after infection with *Borrelia burgdorferi*. "Analysis of joint tissues revealed sustained high levels of IFNγ, CXCL9 and CXCL10 without evidence of joint-localized *B. burgdorferi*, similar to findings in the synovial fluid of patients with post-treatment Lyme disease," Whiteside reports. "We also showed that $CD4^+$ and $CD8^+$ T cells are the major sources of arthritis-promoting IFNγ," she adds.

> "T cell expression of TLR2 contributed to IFNγ production and Lyme arthritis"

Analysis of T cell receptor (TCR) repertoires in T cells from the draining lymph nodes of the *Il10*$^{-/-}$ mice showed that there was no selective expansion of any TCR β-chain V region subsets during *B. burgdorferi* infection. "The use of two different TCR transgenic mice, with specificity towards two distinct non-*Borrelia* epitopes, allowed us to confirm that bystander-activated T cells are contributing to Lyme arthritis," says co-author Janis Weis. "Infection of these TCR transgenic mice with *B. burgdorferi* resulted in the development of arthritis that was dependent on T cells and associated with IFNγ production."

Notably, transcription and expression of the microbial pattern recognition receptor Toll-like receptor 2 (TLR2) was increased on both $CD4^+$ and $CD8^+$ T cells during *B. burgdorferi* infection. Furthermore, T cell expression of TLR2 contributed to IFNγ production and Lyme arthritis. "TLR2 on T cells could act as a co-stimulatory molecule and allow T cells to become activated in an inflammatory or dysregulated environment without TCR recognition," says Whiteside.

The findings support the hypothesis that persistent Lyme arthritis is attributable to an inappropriate inflammatory response as opposed to persistent infection, with potential implications for treatment.

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ORIGINAL ARTICLE Whiteside, S. K. et al. IL-10 deficiency reveals a role for TLR2-dependent bystander activation of T cells in Lyme arthritis. *J. Immunol.* https://doi.org/10.4049/jimmunol.1701248 (2018)