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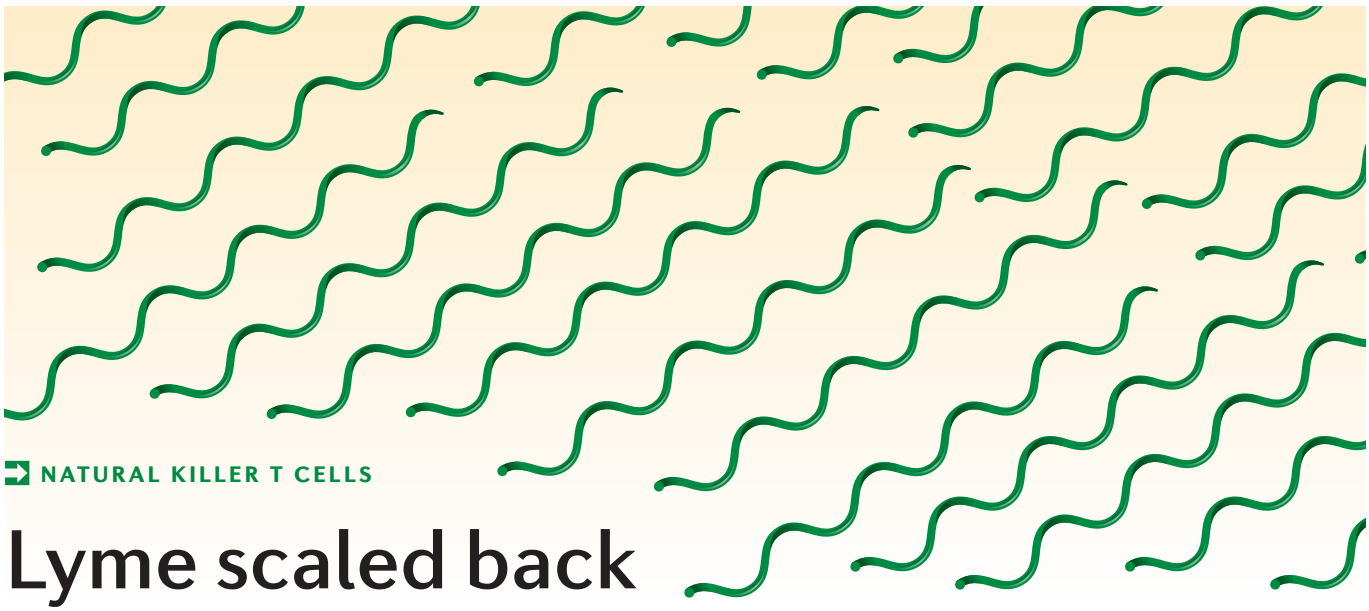

S.Bradbrook/NPG

NATURAL KILLER T CELLS

Lyme scaled back

Invariant natural killer T (iNKT) cells express a restricted T cell receptor repertoire that enables the recognition of pathogen-derived lipid antigens. Much work has focused on how iNKT cells can respond indirectly to pathogens by recognizing microbial lipids displayed on antigen-presenting cells (APCs). A study by Kubes and colleagues now suggests that iNKT cells also respond directly to *Borrelia burgdorferi*, the causative agent of Lyme disease, and prevent bacterial dissemination into the joints.

Previous work by the same group showed that iNKT cells can be activated by liver macrophages to promote an immune response to *B. burgdorferi*. However, this could not explain why iNKT cell-deficient mice infected with *B. burgdorferi* show preferential bacterial accumulation in their joints. The authors used immunohistochemistry and real-time imaging techniques to examine the distribution and behaviour of iNKT cells in the liver and knee joints of mice. In the liver, iNKT cells were exclusively found in blood vessels and showed random crawling behaviour. By contrast, iNKT cells in knee joints were found in the extravascular tissue surrounding blood vessels, were mainly non-motile and predominantly localized to the surface of the knee joint. In frozen sections of human knee joint synovium, iNKT cells were also found outside the vasculature, but fewer iNKT cells were detected in human joints compared with in mouse joints.

> “iNKT cells were directly limiting bacterial dissemination”

Imaging studies of mice infected with fluorescently labelled *B. burgdorferi* showed iNKT cells interacting with bacterial spirochetes at blood vessel walls in the joints. Spirochetes that interacted with iNKT cells subsequently appeared dead, suggesting that the iNKT cells were directly limiting bacterial dissemination. Blocking CD1d (which APCs use to present microbial lipids to iNKT cells) had no effect on *B. burgdorferi* killing, but inhibition of granzymes markedly reduced *B. burgdorferi* killing in the knee vasculature. Thus, iNKT cells in the joint seem to use a granzyme-dependent mechanism to prevent bacterial dissemination. The authors suggest that the reduced frequency of iNKT cells in human joints compared with in mice could explain why *B. burgdorferi* infection leads to Lyme arthritis in humans, but not in rodents.

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ORIGINAL RESEARCH PAPER Lee, W.-Y. *et al.* Invariant natural killer T cells act as an extravascular cytotoxic barrier for joint-invading Lyme *Borrelia*. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1404769111 (2014)