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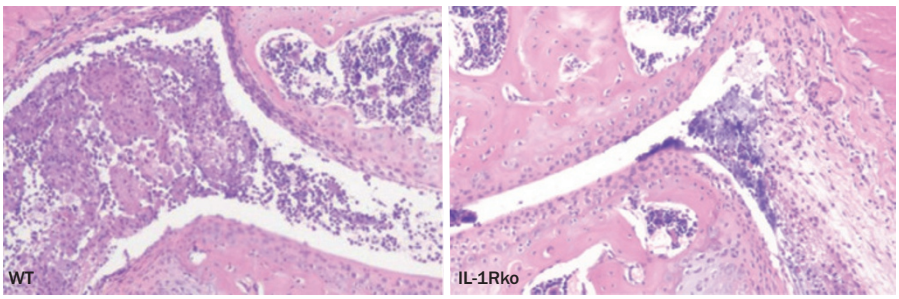
LYME ARTHRITIS

Insight into the innate immune response in Lyme disease

"*Borrelia* spirochetes activate the innate immune response through a TLR2–MYD88-dependent caspase-1 activation that results in IL-1β-driven joint inflammation", say Marije Oosting and Leo Joosten, on the basis of their latest research published in *Arthritis Research & Therapy*.

The investigators generated a new mouse model of Lyme disease, which involved direct injection of *Borrelia burgdorferi* spirochetes into the knee joints of C56Bl/6 mice; this model was then applied in mice lacking expression of certain pattern recognition receptors and components of the inflammasome (also on a C56Bl/6 background) to enable key molecules involved in the immune response to *B. burgdorferi* to be identified.

The central role of IL-1 in the pathogenesis of Lyme disease in mice—as shown previously in human disease—was confirmed: IL-1 receptor knock-out mice were protected against development of Lyme disease, showing considerably reduced joint swelling and reduced influx of inflammatory cells compared with wild-type mice (see figure).



The IL-1R knockout (IL-1Rko) mice are almost completely protected after local exposure to *Borrelia* spirochetes. Note the increased cell influx in wild-type (WT) mice compared with the IL-1Rko mice. Image courtesy of Marije Oosting and Leo Joosten.

Next, Oosting *et al.* studied the response to *B. burgdorferi in vitro* (cytokine production and inflammasome activation by bone marrow-derived macrophages) and *in vivo* in a range of genetically modified mice. In their model, development of Lyme arthritis was shown to require signalling via the TLR2–MYD88 pathway, whereas the NOD1–NOD2–RICK pathways have a minimal role.

Finally the authors report that *B. burgdorferi*-induced production of IL-1, and the development of Lyme disease, require activation of the inflammasome components ASC and caspase-1.

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Original article Oosting, M. *et al*. Murine *Borrelia* arthritis is highly dependent on ASC and caspase-1, but independent of NLRP3. *Arthritis Res. Ther.* **14**, R247 (2012)