SPONDYLOARTHRITIS IL-23 SPECIFICS IN SPONDYLOARTHRITIS

IL-23 induces spondyloarthritis (SpA) in mice by acting on a previously unknown specific subset of cells, ROR- γ t⁺CD3⁺CD4[−]CD8[−] T cells, in the entheses to induce inflammation at this site, according to new research published in *Nature Medicine*.

A link between IL-23 and SpA had already been established—polymorphisms in the IL-23 receptor are associated with ankylosing spondylitis, as well as with increased serum IL-23 concentrations—but the exact role of IL-23 in SpA was unclear. Thus, Sherlock *et al.* investigated whether IL-23 was involved in the development of enthesitis, a key feature of SpA.

Using a collagen antibody-induced arthritis (CAIA) mouse model, the researchers first showed that enthesitis was dependent on IL-23; blocking IL-23 at disease induction reduced both the resulting clinical disease scores and levels of enthesal inflammation in the mice. Next, they confirmed that the entheses contained resident cells that expressed an IL-23 receptor and CD3, but not CD4 or CD8, highlighting them as a key site of action for IL-23.

Importantly, Sherlock *et al.* found that *in vivo* expression of IL-23 alone not only induced enthesitis, but also recapitulated the features of human SpA in mice—characteristic development of inflammation in the entheses and at the aortic root and valve (structurally similar to entheses), as well as enthesal new bone formation.

Finally, the authors further characterized these IL-23-responsive cells. Upon examination, they found that these resident T cells were specifically ROR- γ t⁺CD3⁺CD4[−]CD8[−] and produced IL-22 and IL-17 upon exposure to IL-23 (cytokines already implicated in SpA pathogenesis). Overexpression of IL-22, in particular, in mice led to the induction of bone remodelling.

These data provide a vital insight into the immunopathogenesis of SpA and a future therapeutic target. “The work will encourage those involved in current trials of inhibition of IL-23,” says Hill Gaston, who advised on the study but was not an author. “The identification of an unusual enthesal cell that responds to IL-23 may point to novel therapies that could deplete this population.”

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Original article Sherlock, J. P. *et al.* IL-23 induces spondyloarthropathy by acting on ROR- γ t⁺CD3⁺CD4[−]CD8[−] enthesal resident T cells. *Nat. Med.* **18**, 1069–1076 (2012)