Nature Reviews Rheumatology **10**, 576 (2014); published online 16 September 2014; doi:10.1038/nrrheum.2014.161

EXPERIMENTAL ARTHRITIS

Link between IL-10 and activation of the NLRP3 inflammasome in the synovium

New research in mouse models of inflammatory arthritis shows that IL-10 is a negative regulator of NLRP3 inflammasome components within the inflamed synovium. "Our studies implicate a link between IL-10 and expression of the NLRP3 inflammasome within the inflamed synovium, and advocate a role for IL-10 and inflammasome activation in governing osteoclastogenesis and bone erosion," comments Professor Simon Jones, corresponding author of the study now published in *Arthritis Research & Therapy*.

Activation of the NLRP3 inflammasome has been implicated in various autoimmune and autoinflammatory conditions, but little is known about the regulation of inflammasome components in inflammatory arthritis. IL-10 is an anti-inflammatory cytokine that modulates both innate and cellular immunity through inhibition of signalling via a wide range of pattern recognition receptors, including NLRs. To investigate whether IL-10 is involved in regulation of inflammasome activation in the synovium, the researchers studied antigen-induced arthritis (AIA) in IL-10-knockout and wild-type mice.

> "...the changes in IL-1β expression reflect the capacity of IL-10 to inhibit expression of *Il1b, Nlrp3*..."

Greenhill *et al.* showed that IL-10-knockout mice in the late stages of AIA had an exacerbation of joint pathology in comparison with wild-type mice, and this was associated with increased synovial expression of NLRP3 inflammasome components and increased expression of IL-1β at bone erosion sites, which co-localized with F4/80$^+$ resident macrophages.

They propose that the changes in IL-1β expression reflect the capacity of IL-10 to inhibit the expression of *Il1b, Nlrp3* and genes encoding other inflammasome components. Thus, targeting the inflammasome might be beneficial in diseases with increased IL-1β production, such as osteoarthritis, Muckle–Wells syndrome, and gout. "The use of small-molecule inhibitors that block NLRP3 activity may have downstream therapeutic potential," notes Jones, "and we now need to consider whether this is relevant to human disease."

"Monitoring IL-10 or inflammasome activities within the inflamed joints of patients with early rheumatoid arthritis may prove valuable as a predictor of disease activity or bone erosions," states Jones, "and may help tailor the design of novel treatments for defined patient groups."

Caroline Barranco

Original article Greenhill, C. *et al.* Interleukin-10 regulates the inflammasome-driven augmentation of inflammatory arthritis and joint destruction. *Arthritis Res. Ther.* doi:10.1186/s13075-014-1419-y