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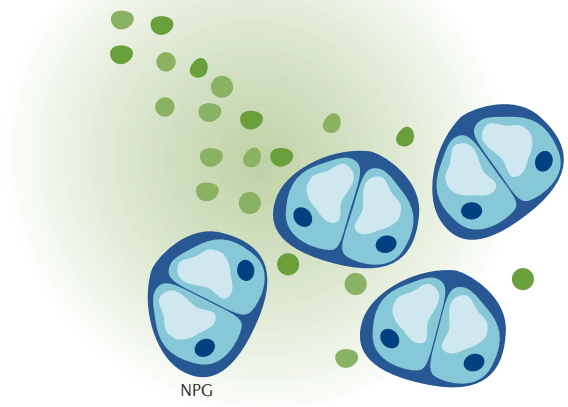
EXPERIMENTAL ARTHRITIS

A protective role for IL-3 in mouse OA

> intra-articular administration of IL-3 was effective in attenuating cartilage breakdown

In a mouse model of post-traumatic osteoarthritis (OA), Mohan Wani and colleagues show that intra-articular injection of IL-3 (a cytokine released by activated T cells) limits damage to cartilage and bone. "IL-3 has a multifaceted role in amelioration of cartilage and subchondral bone damage," asserts Wani, "in addition to modulating the inflammatory response associated with OA."

Previously, these researchers found that IL-3 inhibits osteoclast differentiation *in vitro,* and has indirect, protective effects on cartilage and bone damage in mouse models of inflammatory arthritis.



In the current study, Wani and colleagues showed that the receptor for IL-3 is highly expressed on both mouse and human primary chondrocytes. Under nonpathological conditions, exogenous IL-3 did not affect chondrocyte proliferation, gene expression, or matrix synthesis, nor did its presence affect the differentiation of chondrocytes from cultured human mesenchymal stem cells. By contrast, in the presence of the proinflammatory cytokine IL-1β, IL-3 was able to increase the expression of the chondrocyte specific genes *Sox9* and *Col2a,* which are downregulated by IL-1β in mouse chondrocytes. The presence of IL-3 was also able to reduce the upregulation of the genes encoding matrix metalloproteinases MMP-3 and MMP-13 caused by IL-1β and TNF in both mouse and human chondrocytes. Thus, IL-3 seems to mainly reduce cartilage damage by downregulating the expression of MMPs.

Moving to an anterior cruciate ligament transection mouse model of post-traumatic OA, Wani and colleagues showed that intra-articular administration of IL-3 was effective in attenuating cartilage breakdown, irrespective of whether the cytokine treatment was started before or after the development of OA. Both treatment protocols were able to reduce articular cartilage damage and improve damaged subchondral bone architecture.

According to Wani, "IL-3 has therapeutic potential in amelioration of degeneration of articular cartilage and subchondral bone microarchitecture associated with OA." The team are now planning to conduct studies into the role of IL-3 treatment in a large-animal (dog) model of OA.

Joanna Collison

ORIGINAL ARTICLE Kour, S. *et al.* IL-3 decreases cartilage degeneration by downregulating matrix metalloproteinases and reduces joint destruction in osteoarthritic mice. *J. Immunol.* http://dx.doi.org/10.4049/jimmunol.1500907 (2016)

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