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EXPERIMENTAL ARTHRITIS

Antibody against CSF-1 receptor protects bone and cartilage

Colony stimulating factor-1 (CSF-1; also known as macrophage colony-stimulating factor), is important in the differentiation of cytokine-producing macrophages and bone-resorbing osteoclasts, rendering this growth factor an interesting therapeutic target in rheumatoid arthritis (RA). A study led by Georg Schett now demonstrates that specific blockade of the receptor for CSF-1 (CSF-1R) with a neutralizing antibody not only protects against cartilage and bone destruction, but also has anti-inflammatory effects, in animal models of the disease.

"We decided to block CSF-1R and not CSF-1 itself because IL-34, a cytokine with a similar function to CSF-1, also uses the same receptor," Schett explains. "Therefore, we could neutralize the function of CSF-1 as well as IL-34 in arthritis."

Using a newly generated monoclonal antibody against human CSF-1R, the investigators first confirmed the presence of the receptor in the joints of patients with RA, where they found its expression was increased in comparison with the synovium of patients with osteoarthritis (OA) or healthy individuals. CSF-1R expression was particularly high in those with severe synovitis (regardless of whether they had RA or OA) compared with those with minimal synovitis.

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In patients with RA, CSF-1R was broadly expressed in macrophages, follicular dendritic cells and mature osteoclasts, as well as circulating monocytes and neutrophils. Notably, CSF-1R was found to be expressed on fibroblast-like synoviocytes, which also secrete its ligands IL-34 and CSF-1.

Next, an anti-mouse CSF-1R monoclonal antibody, AFS98, was shown to attenuate erosion of cartilage and bone in both the collagen-induced (CIA) and serum-transfer models of arthritis, in association with depletion of osteoclast numbers but preservation of osteoblasts.

In the CIA model, but not the serum-transfer model, treatment with AFS98 inhibited synovial inflammation, in association with the absence of macrophage infiltration in synovial joints and reduced splenic monocyte recruitment. "These findings contrast with the effects of RANKL blockade in arthritis, which has shown very strong structure-protective effects but not shown effects on inflammation," notes Schett.

Together, the results of specific CSF-1R neutralization with a monoclonal antibody show promise, but await confirmation in studies of human RA.

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Original article Toh, M.-L. *et al.* A CSF-1 receptor monoclonal antibody has potent bone and cartilage protective effects in experimental arthritis. *Arthritis Rheum.* doi:10.1002/art.38624

CORRECTION

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In the Research Highlight of the article by Toh *et al.* published online in *Nature Reviews Rheumatology*, the newly generated monoclonal antibody should be described as specifically targeting human CSF-1R (it is not a human monoclonal antibody and is not AFS98). AFS98 is an anti-mouse CSF-1R monoclonal antibody.