EXPERIMENTAL ARTHRITIS

Fire and ice: syndecan-3 in inflammation

“We found previously that the chemokine CXCL8 is bound to the proteoglycan syndecan-3 on human endothelial cells in rheumatoid synovial tissue,” says Jim Middleton, from the University of Bristol, UK. “These *in vitro* findings suggest that syndecan-3 may be involved in leukocyte trafficking into the rheumatoid synovium”. A paper from Middleton’s group now confirms this finding *in vivo*, and identifies a tissue-specific dual role for syndecan-3 in inflammation.

To examine the role of syndecan-3 in chemokine-driven leukocyte trafficking the researchers injected *Sdc3*^{-/-} and wild-type mice intra-articularly with CXC-chemokine ligand (CXCL) 1 and examined leukocyte migration in the knee. CXCL1 was used as this chemokine is the functional homolog of CXCL8, which rodents lack. Fewer neutrophils accumulated in the joints of *Sdc3*^{-/-} mice than in wild-type mice, and chemokine expression by synovial cells in the knockout mice was also lower.

Next, outcomes from antigen-induced arthritis in *Sdc3*^{-/-} and wild-type mice

were compared: joint swelling, leukocyte accumulation, cartilage degradation and overall disease severity were reduced in the knockout mice compared with wild-type mice. Together, these findings highlight a proinflammatory role for syndecan-3 in inflamed joints.

The researchers also investigated the role of syndecan-3 in other tissues, specifically the skin and cremaster muscle. In contrast to findings in the joint, intradermal injection of CXCL1 resulted in higher levels of neutrophil recruitment in the *Sdc3*^{-/-} mice than in wild-type mice. Similarly, by intravital microscopy, they found that CXCL1 stimulation led to increased leukocyte rolling and adhesion in the cremaster venules in *Sdc3*^{-/-} mice compared with wild-type mice, indicating an anti-inflammatory role for syndecan-3 in these tissues.

“This study shows a novel role for syndecan-3 in inflammation: in the joint it is selectively proinflammatory, but conversely, in the skin and cremaster muscle it is anti-inflammatory,” Middleton explains. He concludes, “Syndecan-3 may

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be an interesting therapeutic target to reduce inflammation and joint destruction in rheumatoid arthritis.”

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Original article Kehoe, O. *et al.* Syndecan-3 is selectively pro-inflammatory in the joint and contributes to antigen-induced arthritis in mice. *Arthritis Res. Ther.* doi:10.1186/ar4610