EXPERIMENTAL ARTHRITIS

Targeting joint lymphatic function

Drainage of excess fluid via the lymphatic system is key for the resolution of acute inflammation, but how important is lymphatic function in the resolution of chronic inflammation? The results reported in a paper by Zhou *et al.* provide a partial answer to this question: in the context of chronic inflammatory arthritis, enhancing lymphangiogenesis and lymphatic drainage can reduce the severity of disease and could have therapeutic potential in this disease.

The authors showed previously that blocking expression of vascular endothelial growth factor receptor 3 (VEGFR-3), which is a receptor for the lymphatic growth factor VEGF-C, inhibited lymphangiogenesis and resulted in more severe disease in a mouse model of chronic inflammatory arthritis (TNF transgenic mice). Here, they tried the opposite approach and overexpressed VEGF-C in the same mouse model.

Recombinant adeno-associated viruses (AAVs) capable of long-term expression of human VEGF-C, or a control virus,

were injected into the joints of 1.5-month-old TNF transgenic mice. The mice were studied over the next 4 months, during which time untreated mice would usually develop arthritis. Synovial volumes, joint deformity, cartilage and bone destruction, and osteoclast numbers were all reduced in the mice treated with AAV-VEGF-C in comparison with the control-treated mice. In addition, the speed of lymphatic flow from inflamed joints to the draining lymph nodes and the extent of lymphangiogenesis were increased in mice from the AAV-VEGF-C group compared with those from the control group.

The authors conclude that therapeutic approaches targeting joint lymphatic function show promise for chronic inflammatory arthritides.

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Original article Zhou, Q. *et al.* VEGF-C attenuates joint damage in chronic inflammatory arthritis by accelerating local lymphatic drainage. *Arthritis Rheum.* doi:10.1002/art.3042