

EXPERIMENTAL ARTHRITIS
NEW SYNOVITIS GENE IDENTIFIED

“Abnormal synovial proliferation is a major characteristic of rheumatoid arthritis; however, the molecular mechanisms behind this process are still unclear and there is no drug that targets it,” explains Ryoji Fujii from the St Marianna University School of Medicine, Kawasaki, Japan. Research from Fujii and colleagues, published in *Arthritis & Rheumatism*, has identified another piece in the puzzle in the shape of *SPACIA1/SAAL1*, a novel gene that they show to be associated with synoviocyte proliferation. Overexpression of *Spacia1* resulted in increased synovitis and worsened disease in collagen-induced arthritis (CIA), a mouse model of rheumatoid arthritis (RA).

First, the authors performed transcriptome analysis of the foot joints of mice with CIA and identified 80 genes that were overexpressed in these mice in comparison with healthy controls. To find genes that were associated with proliferation, the authors performed proliferation assays in cultured RA synovial fibroblasts, using antisense oligonucleotides and small interfering RNAs, and identified *SPACIA1* as the gene that, when blocked, most strongly inhibited RA synovial fibroblast proliferation.

Expression analysis revealed that *SPACIA1* is highly expressed in the hyperplastic synovial lining from patients with RA or osteoarthritis, and that the expression level of this gene directly correlates with the thickness of this lining. In addition, the authors generated transgenic mice that overexpressed *Spacia1*: these mice did not develop arthritis spontaneously, but they developed more severe disease more quickly than the wild-type controls on administration of a lower than usual dose of bovine type II collagen.

“The most significant finding in our paper is that *SPACIA1* is a novel synovitis-related disease-modifying factor,” claims Fujii. “We are now analyzing the *SPACIA1* promoter to determine regulatory factors of *SPACIA1* gene expression and we have generated *Spacia1*-deficient mice to assess whether *Spacia1* is a crucial factor of abnormal synovial proliferation in the CIA model of RA.”

Jenny Buckland

Original article Sato, T. *et al.* Overexpression of *SPACIA1/SAAL1*, a new gene that is involved in synoviocyte proliferation, accelerates the progression of synovitis in mice and humans. *Arthritis Rheum.* doi:10.1002/art30617