COMMENT

Cartilage destruction in rheumatoid arthritis

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Synovial fibroblasts represent an important source of matrix degrading enzymes mediating joint destruction in rheumatoid arthritis.¹ In our search for new pathways for the activation of synovial fibroblasts we have detected endogenous retroviral sequences, like the line 1 element (L1).²

To study the functional role of L1 we transduced synovial fibroblasts with L1 constructs and showed that L1 induces a number of crucial transcription factors for the activation of these cells. Most significant was the induction of p38 δ . At present p38 δ has not been explored in detail, although several interesting pathways have been examined. The fact that p38 δ phosphorylates various transcription factors, including ATF-2, Elk-1, and SAP-1, and that it could be shown that the ATF-2 pathway is potentially linked to the induction of certain oncogenes as well as to the production of matrix degrading metalloproteinases³ has put this molecule at the focus of our interest.

Because inhibition of p38 α and β has been the centre of interest for new therapeutic targets by the industry we studied the expression of the different isoforms at sites of joint destruction⁴ and showed that synovial cells appear to be activated not only by a cytokine dependent pathway but also by a cytokine independent pathway. The latter fact may explain the observation that anticytokine treatments of rheumatoid arthritis do not abolish joint destruction completely.

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