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BONE

An alternative pathway for bone destruction in inflammatory arthritis?

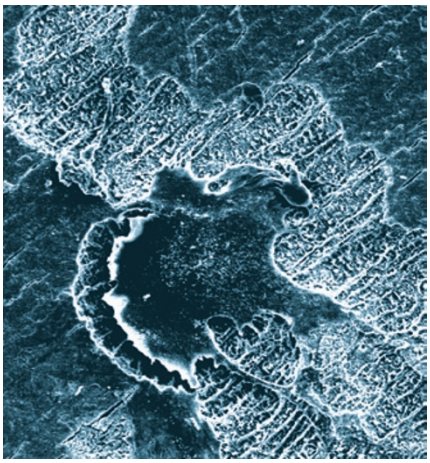
New research points to the role of an alternative osteoclastogenic pathway in the bone destruction observed in inflammatory arthritis—independent of receptor activator of nuclear factor κB ligand (RANKL), a critical mediator of bone resorption—and highlights the key role of synovial fibroblasts in this process.

To enable this discovery, Iannis Adamopoulos and colleagues investigated the function of factors secreted by synovial fibroblasts isolated from patients with rheumatoid arthritis (RA), pyrophosphate arthropathy (PPA) or osteoarthritis (OA). Expression of RANKL and osteoprotegerin (OPG)—factors with opposing roles in osteoclastogenesis; RANKL promotes this process, whereas OPG inhibits it—was also examined in these synovial fibroblasts.

The RANKL:OPG ratio was markedly higher in RA synovial fibroblasts than in OA or PPA fibroblasts. Furthermore, *in vitro* assays showed that soluble factors secreted by RA and PPA synovial fibroblasts can indeed induce osteoclast formation and subsequent bone resorption.

However, when these *in vitro* assays were repeated in the presence of factors that block RANKL, TNF and IL-6 signalling pathways, osteoclast formation and bone resorption were diminished, but not completely abolished. This finding led Adamopoulos and co-workers to reason that other, as yet unidentified, factors act directly on osteoclast differentiation in a manner independent of RANKL, IL-6 and TNF, despite the high RANKL:OPG ratio observed in their study.

"The next step is to define the secreted factors by the synovial fibroblasts," acknowledges senior author Adamopoulos. "Our data do not question the significance of high RANKL expression by RA synovial fibroblasts in bone destruction, but highlight the need for a better understanding of RANKL-independent pathways," he adds.



Osteoclast resorbing bone. Courtesy of I. E. Adamopoulos.

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Original article Dickerson, T. J. *et al.* Rheumatoid and pyrophosphate arthritis synovial fibroblasts induce osteoclastogenesis independently of RANKL, TNF and IL-6. *J. Autoimmunity* doi:10.1016/j/jaut.2012.06.001