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Activation of synovial fibroblasts by resting T cells

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Elena Neumann,[Aff1]

Aff1 University Hospital, Regensburg, Germany

Keywords

Fibroblast activation, resting T cells, rheumatoid arthritis, synovial fibroblasts

Context

Many T cells in the synovial tissue of rheumatoid arthritis (RA) patients do not express characteristics of recently activated T lymphocytes (such as the high affinity interleukin [IL]-2R) but do express the lymphocyte activation markers CD69 and HLA-DR. Paradoxically, synovial T cells are also hyporesponsive to TCR/CD3 stimulation. RA synovial fibroblasts are key players in the erosion of cartilage and bone. The aim of this study was to analyze the ability of resting T cells to activate RA synovial fibroblasts in the absence of mitogens.

Significant findings

Although no evidence for T-cell activation was found, mRNA synthesis of stromelysin, IL-6, IL-8 and other cytokines was upregulated in synovial fibroblasts. $CD4^+$, $CD8^+$, $CD45RA^+$, $CD45RO^+$ cells showed equal effects. A synergistic activation pattern was found when IL-17 was added to the cocultures.

Comments

To date, the tissue destructive behavior of synovial fibroblasts has been thought to be mainly driven by cytokines such as tumor necrosis factor-a and IL-1b that are released from synovial macrophages. The present paper provides a potentially important novel link between resting T cells and synovial fibroblasts in that cocultures of these cells were able to stimulate the synthesis of cytokines, stromelysin

and other activation markers in synovial fibroblasts. Unfortunately, not all synovial fibroblasts of patients with RA showed activation by resting T cells; in about 25% of >20 experiments T cells did not induce appreciable cytokine synthesis. Furthermore, no significant differences could be observed between RA fibroblasts, osteoarthritic synovial or dermal fibroblasts. The following points are of interest and should be addressed in future studies. Do fibroblasts, activated by resting T cells, keep their activation without permanent coculture? Do activated fibroblasts show higher destructive behavior towards cartilage? How can resting T cells activate fibroblasts without being activated themselves? Which factors are involved in fibroblast activation, and what are the molecular mechanisms for this mode of activation?

Methods

Magnetic beads, RT-PCR, RNase protection assay, intracellular cytokine staining, flow cytometry, ELISA, coculture of resting T cells and RA synovial fibroblasts, comparison of autologous and allogeneic cocultures

Additional information

References

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