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IL-1a and arthritis

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Keywords

Arthritis, IL-1a, macrophage, neutrophil

Context

Interleukin (IL)-1 has been implicated in the pathogenesis of rheumatoid arthritis (RA) and is thought particularly to play a central role in joint destruction. Elevated levels of IL-1 are present in the synovial fluid, synovial membrane and cartilage-pannus junction of arthritic joints. The relative contributions of IL-1 and tumour necrosis factor (TNF)-a and the roles of T-cell-independent and antigen-specific T-cell-dependent mechanisms in rheumatoid synovitis are still unclear. The authors investigated the potential direct effect of IL-1a on arthritis in mice transgenic (Tg) for human IL-1a (hIL-1a).

Significant findings

Overexpression of hIL-1a was detected at both the mRNA and protein levels in a wide variety of tissues, including synoviocytes and bone marrow (BM) macrophages. The hIL-1a secreted by synoviocytes and BM macrophages was shown to be biologically active. Synovial hyperplasia (resulting from accumulation of cells with a macrophage-like morphology), loss of cartilage, bone erosion, fibrin deposits and the formation of pannus-like tissue were revealed in 8-week-old mice. Nearly 80% of freshly isolated synoviocytes were positive for the F4/80 antigen. The majority of the cells infiltrating below and within the synovium were polymorphonuclear neutrophils (PMNs) and expressed high levels of Gr-1, indicating they were mature, tissue-degrading PMNs. Granulocyte-macrophage colony-stimulating factor was found to be twofold to threefold higher in supernatants from synoviocytes and BM macrophages and in the sera of Tg mice compared to sera of non-Tg littermates.

Comments

This study provides insight into the role of IL-1 in arthritis. Although several RA models have implicated lymphocytes in the pathogenesis of inflammatory arthritis, very few a/?T-cell receptor$^+$ cells, B220$^+$ cells or CD80$^+$/CD86$^+$ cells were observed in the joints of the hIL-1a Tg mice studied here. The authors speculate that hIL-1a may modulate synoviocytes towards a tissue-destructive phenotype rather than having an antigen-presenting function, implying the development of inflammatory arthritis in a T-cell-independent manner. The relative contributions of IL-1 and TNF-a in RA are difficult to clarify. Distinguishing between the effects of these two cytokines is especially difficult in Tg mice because TNF mRNA was induced in the hIL-1a Tg mice (stated in discussion, but data not shown) and also IL-1 receptor antagonist modulates disease in TNF-Tg mice. The study of the IL-1a transgene on a TNF-deficient background may be one way to clarify the role of IL-1 in RA. It would be interesting to determine, in this Tg mouse model, which other cytokines could play a role in chronic inflammatory arthritis.

Methods

Generation of transgenic mice, cell culture, northern blot analysis, immunoprecipitation, SDS-PAGE, ELISA, bioassay, immunohistochemistry, flow cytometry, histological analysis

Additional information

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