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TRANCE/RANKL in bone erosion in arthritis

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Keywords

Bone erosion, cartilage destruction, osteoclast, serum transfer model, TRANCE/RANKL

Context

Although joint destruction is a complication of severe rheumatoid arthritis (RA), the definitive pathogenic mechanisms have yet to be elucidated. TRANCE/RANKL has been characterized as an essential factor not only for osteoclastogenesis, but also for the viability of dendritic cells resulting in the activation and proliferation of T cells. A significant reduction of bone erosion is seen in the adjuvant arthritis model after blockade of TRANCE/RANKL. To exclude the influence of T cell-dendritic cell interactions on this process, the authors generated inflammatory arthritis in TRANCE/RANKL-deficient mice using a serum transfer model bypassing the requirement for T cell activation.

Significant findings

Following serum transfer, inflammation developed in TRANCE/RANKL knockout mice similarly to matched littermates; however, bone erosion was dramatically reduced in the knockout mice. In contrast, erosion of cartilage could not be prevented. These results suggest that osteoclasts play a critical role in the pathogenesis of bone erosion in RA independent of T cell-dendritic cell interactions, but that the mechanism of cartilage destruction, as well as the factors which drive the inflammatory process, appears to be different from those of bone erosion.

Comments

In contrast to this study, protection from cartilage destruction has been previously reported in the adjuvant arthritic model after blockade of TRANCE/RANKL. As discussed by the authors, these differences in protection from cartilage erosion could be explained by the degree of primary cartilage damage intrinsic to these models. In addition, it has to be considered that various cells, such as monocyte/macrophages, T cells, and synovial fibroblasts (SF), may also contribute to joint destruction in RA. Furthermore, it has been shown that RA-SF can induce osteoclastogenesis by producing TRANCE/RANKL and can release matrix degrading proteases. Thus, cartilage degradation requires a complex interaction between different cell types. The difference in the protection from cartilage erosion in these models is noteworthy and needs to be examined in more detail.

Methods

TRANCE/RANKL-deficient mice, serum transfer model of arthritis, micro CT imaging, haematotoxylin and eosin staining, toluidine blue staining, fluorescent staining

Additional information

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