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Determination of three isoforms of RANKL

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Keywords

Isoform, osteoclastogenesis, RANKL, T cells

Context

RANKL (receptor activator of nuclear factor-?B ligand; also known as osteoprotegerin ligand, osteoclast differentiation factor, tumour necrosis factor-related activation-induced cytokine) induces the differentiation of T cells and osteoclasts. Therefore it has been suggested that the RANK-RANKL pathway plays an important role in cellular interaction at sites of bone destruction in rheumatoid arthritis (RA).

Significant findings

The authors found two new isoforms of RANKL:RANKL2 has a shorter intracellular domain than the original RANKL, and RANKL3 lacks a transmembrane domain. Although mRNAs for all three isoforms were detected in both the bone marrow cell line ST2 and the preosteoblastic cell line MC3T3-E1, only the expression of RANKL2 was suppressed by treatment with 1a,25-dihydroxyvitamin D_3 and dexamethasone. In thymus, $CD4^-CD8^-$, $CD4^+CD8^-$ and $CD4^-CD8^+$ cells expressed all three isoforms of RANKL, but RANKL2 could not be detected in $CD4^+CD8^+$ cells. These results suggest that the regulation of osteoclastogenesis and T-cell differentiation by RANKL might be more complex than previously thought.

Comments

In RA, activated T cells, synovial fibroblasts and bone marrow derived cells express RANKL. Treatment with 1a,25-dihydroxyvitamin D_3 is known to be essential for the induction of osteoclast differentiation by RA synovial fibroblasts, and the authors suggest that the expression of the RANKL

isoforms is differentially regulated by 1a,25-dihydroxyvitamin D_3. Moreover, the soluble isoform of RANKL (RANKL3) produced by activated T cells could induce osteoclast differentiation.

Since RANKL is important both in osteoclast and T-cell differentiation, further studies on the function and regulation of RANKL isoforms might help to clarify the mechanism of bone resorption in inflammatory diseases such as RA.

Methods

Northern hybridization, RT-PCR, transfection, immunofluorescence

Additional information

References

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