

Poster Abstract

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IL-33 inhibits osteoclast formation in vitro through two independent mechanisms

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IL-33 is the most recently discovered pro-inflammatory cytokine of IL-1 family, which is closely related to IL-18, a powerful osteoclast (OC) inhibitor. The receptor for IL-33 is ST2L, a membrane-bound receptor and ST2, a soluble decoy receptor with anti-inflammatory properties.

We have found that IL-33 is also a powerful OC differentiation inhibitor, blocking OC formation in RANKL/M-CSF stimulated mouse spleen cells or bone marrow cells. IL-33 did not inhibit OC formation from RANKL stimulated RAW264.7 cells or from highly enriched OC progenitor pools such as bone marrow-derived macrophages (BMM), suggesting IL-33 may not act directly on OC progenitors. However, IL-33 inhibits OC formation of BMM co-cultured with osteoblastic cells (Kusa O or primary osteoblasts) stimulated by $1\alpha,25$ (OH)₂ Vitamin D₃. This suggests mediation of IL-33 action by osteoblastic cells. Separating osteoblasts from BMM by semipermeable membrane did not ablate IL-33 action, suggesting mediation by a soluble inhibitor. This was shown not to be OPG.

In addition to osteoblasts, T cells also mediated IL-33 inhibitory action when added to RANKL/M-CSF stimulated BMM cultures. In cultures containing T cells, IL-33 strongly induced mRNA expression of osteoclast inhibitors IL-4 and IL-13 as well as IL-5.

In summary, IL-33 is a novel osteoclast formation inhibitor with at least to two independent mechanisms of IL-33 inhibition i.e. via T cells and via osteoblastic cells.