Interleukin-32 Promotes Osteoclast Differentiation but Not Osteoclast Activation

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Résumé en anglais	BackgroundInterleukin-32 (IL-32) is a newly described cytokine produced after stimulation by IL-2 or IL-18 and IFN-γ. IL-32 has the typical properties of a pro-inflammatory mediator and although its role in rheumatoid arthritis has been recently reported its effect on the osteoclastogenesis process remains unclear. Methodology/Principal Findings In the present study, we have shown that IL-32 was a potent modulator of osteoclastogenesis in vitro, whereby it promoted the differentiation of osteoclast precursors into TRAcP+ VNR+ multinucleated cells expressing specific osteoclast markers (up-regulation of NFATc1, OSCAR, Cathepsin K), but it was incapable of inducing the maturation of these multinucleated cells into bone-resorbing cells. The lack of bone resorption in IL-32-treated cultures could in part be explain by the lack of F-actin ring formation by the multinucleated cells generated. Moreover, when IL-32 was added to PBMC cultures maintained with soluble RANKL, although the number of newly generated osteoclast was increased, a significant decrease of the percentage of lacunar resorption was evident suggesting a possible inhibitory effect of this cytokine on osteoclast activation. To determine the mechanism by which IL-32 induces such response, we sought to determine the intracellular pathways activated and the release of soluble mediators in response to IL-32. Our results indicated that compared to RANKL, IL-32 induced a massive activation of ERK1/2 and Akt. Moreover, IL-32 was also capable of stimulating the release of IL-4 and IFN-γ, two known inhibitors of osteoclast formation and activation. Conclusions/Significance This is the first in vitro report on the complex role of IL-32 on osteoclast precursors. Further clarification on the exact role of IL-32 in vivo is required prior to the development of any potential therapeutic approach.
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