Rheumatoid arthritis is characterised by osteoclast-mediated bone loss. In several studies it was shown that SHIP-/- mice are severely osteoporotic due to increased numbers of hyperreactive osteoclasts. Because SHIP is part of the signalling pathway of the inhibitory FcγRIIB, the aim of this study was to investigate the role of FcγRIIB in osteoclastogenesis and osteoclast function.

Compared with wild-type mice, bone erosion and cathepsin K staining were clearly enhanced during antigen-induced arthritis in the knee joints of mice deficient for the inhibitory FcγRIIB. FACS analysis of in vitro differentiated osteoclasts showed that FcγRIIB expression was not significantly different on osteoclasts compared with macrophages, whereas all activating FcγR classes were strongly downregulated. However, expression levels of all FcγR classes were high on all bone marrow subsets prone to differentiate towards osteoclasts, as discriminated by double-staining for ER-MP20/ER-MP12. The composition of these bone marrow subsets was similar for both FcγRIIB-/- mice and C57Bl/6 wild-type controls. Bone marrow-derived osteoclasts of FcγRIIB-/- mice and wild-type controls showed no differences in the number of tartrate-resistant acid phosphatase + (TRAP+) cells and mRNA expression of the osteoclast markers cathepsin K, CTR, DC-STAMP and NFATc1. In line with this, no differences were observed in the formation of resorption pits on bone. In the presence of immune complexes, differentiation of both FcγRIIB-/- and wild-type osteoclasts resulted in significantly reduced numbers of large TRAP+ cells (containing more than 10 nuclei), but not of smaller sized osteoclasts (3–10 nuclei). The immune complex (IC)-mediated reduction in osteoclast size resulted in decreased mRNA expression of osteoclast markers and reduced resorption pit formation on bone, showing that small osteoclasts resorb bone less efficiently than large ones. TRAP staining of arthritic knee joints displayed significantly enhanced numbers of TRAP+ osteoclasts in FcγRIIB-/- mice compared with wild-type controls. Interestingly, these osteoclasts were smaller than the ones found in wild-type mice.

This study shows that IC inhibit osteoclastogenesis, resulting in the formation of smaller sized osteoclasts and decreased osteoclast function. Furthermore, using FcγRIIB-/- mice, we demonstrated that the inhibitory effect of IC is not directly mediated by FcγRIIB. However, high levels of activating FcγR on bone marrow precursors prone to differentiate towards osteoclasts suggest that IC exert their inhibitory effect at an early phase of differentiation via activating FcγR.
Immune complex-mediated inhibition of osteoclastogenesis: role for the inhibitory Fc receptor IIβ in bone erosion in antigen-induced arthritis?

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Ann Rheum Dis 2010 69: A23
doi: 10.1136/ard.2010.129593s

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