A57 IMMUNE COMPLEX-MEDIATED INHIBITION OF OSTEOCLASTOGENESIS: ROLE FOR THE INHIBITORY FC γ RECEPTOR IIB IN BONE EROSION IN ANTIGEN-INDUCED ARTHRITIS?

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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 Fc γ RIIB, the aim of this study was to investigate the role of Fc γ RIIB 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 Fc γ RIIB. FACS analysis of in vitro differentiated osteoclasts showed that Fc γ RIIB expression was not significantly different on osteoclasts compared with macrophages, whereas all activating Fc γ R classes were strongly downregulated. However, expression levels of all Fc γ R 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 Fc γ RIIB^{-/-} mice and C57Bl/6 wild-type controls. Bone marrow-derived osteoclasts of Fc γ RIIB^{-/-} 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 Fc γ RIIB^{-/-} 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 Fc γ RIIB^{-/-} 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 Fc γ RIIB^{-/-} mice, we demonstrated that the inhibitory effect of IC is not directly mediated by Fc γ RIIB. However, high levels of activating Fc γ R on bone marrow precursors prone to differentiate towards osteoclasts suggest that IC exert their inhibitory effect at an early phase of differentiation via activating Fc γ R.