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Molecular analysis of expression and function of hFcgammaRIIbl and b2 isoforms in myeloid cells.

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Abstract

The inhibitory receptor FcgammaRIIb becomes tyrosine phosphorylated and associates with the inositol phosphatase SHIP to downregulate phagocytosis. The two splice variants of FcgammaRIIb, b1 and b2, are differentially expressed in hematopoetic cells. Both isoforms of FcgammaRIIb are expressed in human myeloid cells although FcgammaRIIb2 predominates. In murine B cells FcgammaRIIb2 associates with clathrin-coated pits and undergoes endocytosis, whereas FcgammaRIIbl is excluded from the coated pits, indicating that the two isoforms serve partially differing functions. In humans, there are conflicting reports with regard to the ability of FcgammaRIIb2 to become tyrosine phosphorylated, and the functional capacities of the two isoforms are poorly understood. We, and others, have previously reported that the expression of FcgammaRIIb is upregulated in human monocytes by the anti-inflammatory cytokine IL-4. Here, we extend these findings to demonstrate that the IL-4-induced upregulation of FcgammaRIIb is synergistically enhanced by the addition of IL-10, both at the protein and the mRNA level. The upregulated receptors are functional as assessed by their ability to become tyrosine phosphorylated and to downregulate phagocytosis. Interestingly, both b1 and b2 isoforms are upregulated by anti-inflammatory cytokines. Transfection experiments expressing human FcgammaRIIbl or b2 in Raw 264.7 murine macrophage cells revealed that both isoforms are tyrosine phosphorylated and promote SHIP phosphorylation. Finally, both b1 and b2 isoforms of FcgammaRIIb downregulate phagocytosis to a similar extent. Thus we conclude that FcgammaRIIbl and b2 are both functional inhibitory receptors in the phagocytic process.

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