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IL-4Rα, A NEW MEMBER THAT ASSOCIATES WITH SYK KINASE: IMPLICATION IN IL-4- INDUCED HUMAN NEUTROPHIL FUNCTIONS.

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Although Syk has been reported to be associated with IL-2Rα and IL-15Rα in some hematopoietic cells, its association has never been investigated in the IL-4/IL-4R system. Here, we demonstrate for the first time that Syk is constitutively associated with IL-4Rα in human PMNs and that IL-4 stimulation increases the amount of Syk associated with IL-4Rα. Moreover, upon IL-4 treatment, a pool of Syk associated with IL-4Rα is phosphorylated. We also report that such association is not unique to PMNs since Syk associates with IL-4Rα in Raji and in PBMC cells. Stimulation of PMNs by IL-4 increased the amount of Syk associated with PLC-β2, pAkt and α-tubulin. Pre-treatment of cells with the Syk-selective inhibitors piceatannol or Syk inhibitor II significantly inhibited the ability of IL-4 to enhance phagocytosis, cell adhesion and to delay apoptosis and these results correlate with the ability of piceatannol and Syk inhibitor II to reduce Syk activation and its association with IL-4Rα. Downregulation of Syk by antisense techniques demonstrates the importance of Syk in the antiapoptotic effect of IL-4. We conclude that association of Syk to IL-4Rα is of biological significance and that IL-4Rα is a new candidate to be added to the few cytokine receptor components which associate with Syk.