

P018 The Lipid Phosphatase SHIP regulates SDF-mediated Responses.

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The SH2 domain-containing inositol polyphosphate 5-phosphatase (SHIP) is known to play an important role in the negative regulation by FcγRIIb of PI3K-dependent signalling cascades activated by the B cell antigen receptor (BCR) as well as several tyrosine-kinase coupled cytokine receptors. However, to date the role of SHIP in the regulation of PI3K-dependent signals elicited by GPCR's such as chemokine receptors have not been investigated. In this study, we report that ligation of CXCR4 by SDF-1 has no effect on the tyrosine phosphorylation of SHIP in the murine B cell lymphoma A20. However, FcγRIIb co-ligation inhibits the PI3K-dependent phosphorylation of PKB and ERK1/2 in response to SDF-1. We have also utilised a constitutively active membrane-localised SHIP mutant expressed in the Jurkat leukaemic T cell line, which do not normally express SHIP, to look at the effect of this mutant on SDF-1 stimulated PI3K-dependent signalling events. Experiments have revealed that SDF-1-mediated PKB phosphorylation, chemotaxis and lipid accumulation are inhibited in the presence of this SHIP mutant. Thus, it appears that activation of SHIP can impinge on signalling pathways activated by GPCR's.