

P002 PI3K and the PH domain adaptor Bam32/DAPP1 regulate B lymphocyte antigen presentation and T cell-dependant antibody responses

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Phosphoinositide 3-kinases (PI3Ks) play critical roles in B cell receptor (BCR) signaling in part by mobilizing PH domain signaling proteins such as Bam32/DAPP1. BCR ligation induces PI3K-dependant recruitment of Bam32 to the plasma membrane via its PH domain where it accumulates within F-actin-rich membrane ruffles, BCR caps and BCR-containing endocytic structures. Bam32 membrane recruitment is enhanced rather than inhibited by the inositol 5-phos-phatase SHIP, indicating that its dependant on PI(3,4)P₂ rather than PI(3,4,5)P₃. Both Bam32-deficient and p110 δ -D910A B cells show a significant impairment in BCR-mediated presentation of antigen to T cells. In contrast, these cells have normal antigen-induced BCR internalization and normal ability to present allo-MHC antigen to T cells, suggesting that these molecules affect trafficking or processing of the BCR-antigen complex, rather than antigen uptake or immune synapse formation. In the case of Bam32-deficiency, the impairment in BCR-mediated antigen presentation is overcome by pre-activating cells through CD40, while the impairment of p110 δ -D910A B cells cannot be recovered by any pre-activation tested. Bam32-deficient mice have impaired T cell-dependent B cell responses to protein antigen *in vivo*, as assessed by germinal centre responses and antibody affinity maturation. Our results implicate p110 δ and Bam32 in coordinating receptor trafficking events important for T-dependant antibody responses.