

**P017** Vav proteins are required for ERK but not PI3-K activation following IgM crosslinking but are required for PI3-K activation in response to CD19 signalling

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B cell responses are initiated upon cross-linking of membrane immunoglobulin (mIg) by antigen. CD19 is an example of a coreceptor that amplifies and regulates responses to mIg crosslinking. We show Vav1 and Vav2 proteins regulate Ca<sup>2+</sup> flux and ERK activation in a PI3K independent manner when mIg is crosslinked through IgM. By contrast, upon CD19 engagement both ERK and PI3K activation required Vav1 and Vav2 proteins. Moreover, inhibition of PI3K enzymatic activity or deletion of Vav1 and Vav2 proteins has a much more profound inhibitory effect on Ca<sup>2+</sup> fluxes when the mIg is coligated with CD19 compared with ligation of IgM alone. Our results show the p110 $\delta$  catalytic subunit and the p85 $\alpha$  regulatory subunit have an important contribution to the total PI3K activity elicited by IgM or mIg/CD19 co-ligation. However, IgM stimulated ERK activation is much less dependent upon p110 $\delta$  and p85 $\alpha$  than is mIg/CD19 stimulated ERK activation. Our results indicate that other PI3Ks, possibly p110 $\alpha$ , contribute to PI3K activity in B cells. In addition, we show that CD19 not only enhances B cell responses but also modifies them in a qualitative manner.