

P021 Function of the Gab-2-PI3K pathway in IL-3 signalling
Bridget Fox, Christine Edmead and Melanie Welham
*Department of Pharmacology, University of Bath, Bath,
BA2 7AY, UK*

We have previously demonstrated that class I_A PI3Ks play an important role in regulating IL-3-driven proliferation of BaF/3 cells and have identified Gab-2 as a major binding partner for the p85 regulatory subunit of PI3Ks. We have now investigated the role of Gab-2 in recruitment and function of class I_A PI3Ks in IL-3 signalling. Expression of a Gab-2 variant in which all three p85 binding sites were mutated decreased IL-3-induced proliferation, concomitant with a reduction in activation of PKB and ERK. These effects are similar to those observed in Δp85-expressing clones indicating that disruption of Gab2-PI3K interactions abrogates signals downstream of PI3Ks. However, expression of wild type Gab-2 only partially rescued the defect in IL-3 signalling in cells expressing Δp85 suggesting that Gab-2 may not be the sole method of regulation of PI3Ks in IL-3 signalling. Inhibition of class I_A PI3Ks by Δp85 extended cell cycle times and decreased expression of cyclins D2, D3 and E. Overall, these data support a role for Gab-2 in the recruitment of class I_A PI3Ks which then function to regulate optimal progression of haemopoietic cells through the cell cycle in response to IL-3. Our data also indicate that Gab2-independent pathways may also make a functional contribution.