

## **Defective Proliferation in T Lymphocytes Lacking the p85 $\alpha$ and p85 $\beta$ Regulatory Subunits of PI 3-Kinase**

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PI 3-Kinase activity has been implicated to be essential for lymphocyte survival, proliferation and function. Initially these observations were based largely on the use of overexpression and dominant negative studies, which pointed to the importance of Class IA PI 3-Kinases. More recently, targeted deletion of the predominant Class IA regulatory isoform p85 $\alpha$  has been demonstrated to inhibit B lymphocyte development and function, while T lineage cells were unaffected. Likewise, T cells deficient in p85 $\beta$ , the other expressed regulatory isoform, were able to develop and actually showed enhanced proliferation in response to some stimuli. The question of whether Class IA regulatory subunits of PI 3-Kinases are required in T lymphocyte development, proliferation, and function is thus largely unanswered. To test the hypothesis that these two genes play necessary but redundant roles, we have generated mice bearing a floxed allele of p85 $\alpha$  and a p85 $\beta$  null allele, and bred these conditional double knockouts with mice that express Cre recombinase under the control of the Lck promoter. Agreeing with the notion that Class IA PI 3-Kinases are essential for lymphocyte function, T cells lacking p85 $\alpha$  and p85 $\beta$  show profound defects in activation and proliferation. Surprisingly however, T cell development seems largely unperturbed in these mice. Ongoing studies from this system are presented, with the goal of further clarifying the significance of PI 3-Kinases in immune function.