

**P001** Role of Class IA PI3K in T Cell Function and Autoimmunity

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The class IA subgroup of phosphoinositide 3-kinase (PI3K) is essential for development and function of B cells and mast cells. In T cells, loss of p110 $\delta$  function causes selective defects in signaling and function *in vitro*. However, *in vivo* T cell function in murine loss-of-function models has been difficult to interpret due to redundancy and effects on other cell types. Here we analyze compound mutant mice in which class IA PI3K signaling is abrogated specifically in thymocytes and T cells. Although T cell development is largely unperturbed, peripheral T cells show selective impairments in proliferation and cytokine production *in vitro*. *In vivo*, T cell help to B cells is diminished but antiviral immune responses are retained. Unexpectedly, mice with class IA-deficient T cells develop autoimmune destruction of the lacrimal glands and exhibit other cardinal features of the human disease Sjögren's syndrome. These findings provide definitive evidence that class IA PI3K is essential for a subset of T cell functions, and demonstrate that reduced class IA PI3K signaling in T cells can lead to organ-specific autoimmunity.