

P003 P110 δ is required for innate immunity to allografts and tumours.

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Natural Killer (NK) cells are lymphocytes of innate immunity that kill tumour cells and participate in the rejection of allografts, without prior stimulation. A balance of activating and inhibitory signals regulates NK cell cytotoxicity, but molecular mechanisms are not fully understood. General inhibitors of Phosphoinositide 3-kinase (PI3K) suppress cytotoxicity in human and mouse NK cells. However, which isoforms and how they regulate NK cell activation is unknown, and no data have been published on mice carrying PI3K mutations. P110 δ expression is restricted to leucocytes, where it plays central roles in lymphocyte development and signalling. We have used P110 δ gene-targeted mice in order to determine the role of PI3K in NK cell biology. We show here that P110 δ is required to kill allogeneic cells, but not tumour cells. In line with the *in vitro* data, P110 δ mutant mice failed to fully reject allogeneic cells but, unexpectedly, also transplanted lymphomas. Our data show for the first time a critical role for P110 δ in NK cell rejection of allografts and tumours.