

P041 Role of the phosphoinositide 3-kinase p110 δ in regulation of type 2 cytokine responses and allergic airway inflammation

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We examined the effect of genetic inactivation of the hemopoietic cell-restricted PI3K isoform p110 δ on systemic cytokine and chemokine responses and allergic airway inflammation. Type 2 cytokine responses (IL-4, IL-5 and IL-13) are significantly decreased in p110 δ mutants, whereas Type 1 cytokine responses (IFN γ and CXCL10) were similar or elevated. Elevated IFN- γ production during the primary response to ovalbumin was associated with reduced production of the regulatory cytokine IL-10. IFN- γ and IL-10 production normalized after secondary OVA immunization; however Type 2 cytokine production was persistently reduced. Type 2 cytokine-dependent airway inflammation elicited by intranasal challenge with OVA was dramatically reduced, with reduced levels of eosinophil recruitment and mucus production observed in the lungs. Induction of respiratory hyper-responsiveness to inhaled methacholine, a hallmark of asthma, was markedly attenuated in p110 δ -inactivated mice. Adoptive transfer of OVA-primed splenocytes from normal, but not p110 δ -inactivated mice, could induce airway eosinophilia in naïve, airway-challenged recipient mice. These data demonstrate a novel role for p110 δ in regulation of Type 2 responses and may offer a new therapeutic target for Th2-mediated airway disease.