

P048 The roles of p110 α and p110 δ in B cell development
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Class IA PI3Ks are activated downstream of a variety of tyrosine linked receptors and are crucial to lymphocyte development and function. In mammals, class IA PI3Ks consist of a catalytic subunit (p110 α , p110 β or p110 δ), in complex with one of five regulatory subunits (p85 α , p55 α , p50 α , p85 β or p55 γ). Here we use mice expressing a catalytic inactive form of p110 δ (D910A) or p110 α (D933A) to investigate the extent of redundant versus isoform-specific functions of p110 δ and p110 α . p110 δ ^{D910A/D910A} mice have impaired development of B cells, undetectable marginal zone (MZ) B cells and reduced follicular (FO) B cells. Unlike p110 δ ^{D910A/D910A} mice, homozygous p110 α ^{D933A/D933A} mice are embryonically lethal. Haploinsufficiency of p110 α on its own does not affect B cell development. However, when crossed with p110 δ ^{D910A/D910A} mice, haploinsufficiency of p110 α further impairs the B cell development, dramatic reduction of FO B cells. Moreover, p110 δ ^{D910A/D910A};p110 α ^{WT/D933A} compound mutant mice have dramatically reduced numbers of newly arrived immature B cells in the spleen and the transition of B cells through crucial checkpoints during maturation is also affected. Our results indicate a functional redundancy between p110 δ and p110 α during FO B cell development, whereas marginal zone B cell development appears to depend exclusively on p110 δ .