

P031 The Epistatic Relationship between PTEN and the PI3K Catalytic Subunit p110 δ in B cell Development
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PI3K and PTEN act in direct opposition to each other by regulating the levels of the second messenger PIP₃, a major effector of the PI3K pathway. Mice in which either PI3K or PTEN function have been disrupted display a number of B cell defects, including altered B1 and Marginal Zone B cell lineages. We have analysed the relationship between the PI3K catalytic subunit p110 δ and PTEN by generating a mouse line in which both alleles are disrupted in the B cell compartment simultaneously. Whilst the B1 cell population in these double mutant mice was restored to wildtype levels, the numbers of MZ B cells was found to be intermediate between wildtype and PTEN deficient mice. We show that PKB phosphorylation is significantly increased in double mutant B cells compared to wildtype and that there is a direct correlation between PKB activity and the number of MZ B cells. Altered MZ B cell numbers are not due to a survival defect as demonstrated through BrdU labelling studies and the inability of the p110 δ ^{-/-} phenotype to be rescued by a *bcl-2* transgene. Finally, the lymphoproliferative syndrome observed in aged PTEN^{+/-} mice failed to be ameliorated in the absence of p110 δ . Our results demonstrate an epistatic relationship between PI3K and PTEN, which acts to maintain a signalling balance for normal B homeostasis and differentiation. Although p110 δ is a significant PI3K catalytic isoform in B lymphocytes, the additional contribution from other isoforms is also recognised and discussed.