

P001 Recovery from lupus-like disease following PI3K γ deletion
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Systemic lupus erythematosus is a multigenic disease characterised by activation of autoreactive T cells, B cells and macrophages. Autoreactive B cells induce an increase in circulating autoantibodies. As the disease progresses, mesangial proliferation and autoantibody accumulation in the kidney cause glomerulonephritis and renal failure. We previously described the phenotype of mice expressing an activating mutation of the class IA PI3K p85 regulatory subunit, p65PI3K, in T cells. These mice show prolonged activation of CD4⁺ memory T cells, giving rise to a CD4⁺ lymphoproliferative disorder, secondary B cell activation, and generation of a lupus-like disease. Class IB PI3K γ is an enzyme activated by G protein-coupled receptors, including chemokine receptors. PI3K γ deletion results in inhibition of neutrophil and macrophage migration. In light of the role of these cells in inflammation, we analysed whether PI3K γ deficiency impaired development of lupus-like disease in p65PI3K transgenic mice. We show that PI3K γ -deficient p65PI3K Tg mice remain healthy for prolonged periods. They exhibit lymphoproliferation, but are protected from development of lupus-like disease. Our observations support a potential role for PI3K γ as a therapeutic target for systemic lupus erythematosus.