PI3K? deficiency delays the onset of experimental autoimmune encephalomyelitis and ameliorates its clinical outcome.

Abstract:
PI3Ks control signal transduction triggered by growth factors and G-protein-coupled receptors and regulate an array of biological processes, including cellular proliferation, differentiation, survival and migration. Herein, we investigated the role of PI3K? in the pathogenesis of EAE. We show that, in the absence of PI3K? expression, clinical signs of EAE were delayed and mitigated. PI3K?-deficient myelin oligodendrocyte glycoprotein (MOG)(35-55)-specific CD4(+) T cells appeared later in the secondary lymphoid organs and in the CNS than their WT counterparts. Transfer of WT CD4(+) cells into PI3K?(-/-) mice prior to MOG(35-55) immunisation restored EAE severity to WT levels, supporting the relevance of PI3K? expression in Th cells for the pathogenesis of EAE; however, PI3K? was dispensable for Th1 and Th17 differentiation, thus excluding an altered expression of these pathogenetically relevant cytokines as the cause for ameliorated EAE in PI3K?(-/-) mice. These findings demonstrate that PI3K? contributes to the development of autoimmune CNS inflammation.