

P008 Cell-mediated immunity is dependent on Inhibitory- κ B kinase (IKK) α activity

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The I- κ B kinase (IKK) complex regulates the activation of NF- κ B a key transcription factor in inflammation and immunity. Whilst IKK β activity is necessary for pro-inflammatory and anti-apoptotic gene expression, IKK α has distinct roles in lymphorganogenesis and B cell maturation. Here we describe a role for IKK α in cell mediated immunity (CMI). Paw inflammation in methylated BSA-induced CMI was significantly reduced in transgenic mice expressing a mutant IKK α protein that cannot be activated (Ikk $\alpha^{AA/AA}$) compared to wild-type (WT). Antigen-induced Ikk $\alpha^{AA/AA}$ splenocyte IL-2 and IFN γ production were also significantly reduced *ex vivo*, but could be normalised by using WT T cell: Ikk $\alpha^{AA/AA}$ dendritic cell (DC) but not Ikk $\alpha^{AA/AA}$ T cell:WT DC combinations. This suggests Ikk $\alpha^{AA/AA}$ DCs can present antigen and prime T cells and that reduced CMI is due to an intrinsic defect in Ikk $\alpha^{AA/AA}$ T cells as opposed to DCs. However, LPS-induced production of the important Th1 cytokine IL-12 is impaired in Ikk $\alpha^{AA/AA}$ DCs. We are currently addressing the hypothesis that IKK α activity may be required for the generation and maintenance of antigen-specific T cells *in vivo*.