

Itk is crucial for early IL-4 production and Th2 differentiation
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The Tec family tyrosine kinase, Itk, plays an important role in TCR signaling. Studies of CD4⁺ T cells from Itk-deficient mice have demonstrated that Itk is critical for the activation of PLC- γ 1, leading to calcium mobilization in response to TCR stimulation. Additional *in vivo* studies have demonstrated that in response to a variety of different pathogens, Itk-deficient mice can elicit a Th1 response, albeit weaker, while they completely fail to elicit Th2 responses. In some instances, Itk-deficient mice elicited a Th1 response to a pathogen that induced a Th2 response in wild type counterparts. To further elucidate the role of Itk in CD4⁺ cell differentiation, we crossed Itk^{-/-} mice to 5C.C7 Rag^{-/-} mice and examined T cell differentiation in non-skewing conditions in response to varying concentrations of antigenic peptide and altered peptide ligands. Interestingly, in situations that induce wild type cells to differentiate towards the Th2 lineage, Itk-deficient cells always differentiate into Th1 effector cells. Given exogenous cytokine, however, Itk-deficient cells possess the capacity to fully differentiate into either Th1 or Th2 effector cells. Nevertheless, Itk-deficient Th1 and Th2 cells possess defects in IFN- γ and IL-4 production, respectively. Furthermore, in wild type cells we have found Itk mRNA and protein to be upregulated in *in vitro*-differentiated Th2 cells compared to Th1. Together these studies suggest an important role for Itk in cytokine production and T helper cell differentiation.