A ROLE FOR ITK IN CD8 T CELL DEVELOPMENT AND FUNCTION

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ITK [IL-2 Inducible T cell Kinase] is a member of the TEC family of tyrosine kinases. In CD4 T cells, ITK is important for the efficient activation of PLC□, the generation of a sustained calcium flux and the activation of ERK/MAPK kinases downstream of TCR signalling.

In the absence of ITK, although there is no appreciable change in the cellularity of peripheral lymphoid organs, the CD4: CD8 ratio is reduced to 1:1. This is reflected in a change in total CD4 but not CD8 T cell numbers in the periphery. In addition a majority of the CD8 T cells in ITK deficient mice exhibit an activated, memory phenotype in that they are mostly CD44hi, CD122hi and Ly6Chi.

We find that there is a slow but appreciable increase in the percentages and total numbers of mature and activated CD8 T cells in the thymus of ITK deficient mice. In addition, the CD8 T cells in these mice are impaired in the responses downstream of TCR cross-linking, and are also impaired in the generation of an effective immune response to infection with LCMV.