National Human Genome Research Institute (NHGRI)

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Tec Kinase Deficient Mice

NHGRI invention number:
E-178-2003

Key Words
Tec kinase, T-Cell, T Cell Receptor, Cytokines, Rlk, Itk

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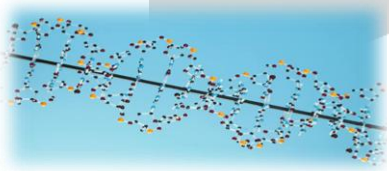

Summary
Stimulation of T lymphocytes through the T Cell Receptor (TCR) elicits broad responses required for proper immune function, including cell proliferation, cytokine production and apoptosis. We have developed transgenic mice to address the roles of Tec nonreceptor kinases Rlk and Itk in TCR signaling. Rlk-deficient mice and Rlk/Itk double-deficient mice have defects in TCR responses including proliferation, cytokine production and apoptosis *in vitro* and adaptive immune response to infectious agents *in vivo*. Cells from these mice indicate that these kinases are critical for proper regulation of phospholipase C, calcium mobilization and ERK activation, as well as activation of downstream transcription factors in response to TCR stimulation. These models also show abnormal production of cytokines by type 1 and type 2 T helper (Th1 and Th2) cells. Defects in T cell function are minor in Rlk-deficient animals but greatly enhanced in Rlk/Itk double-deficient mice.

Potential Commercial Applications
These mice provide a useful model for dissecting out the complex interactions of TCR signaling. Additionally, they can serve in evaluation of therapeutics directed at specific classes of diseases (Th1- or Th2-driven) and of potential global Tec kinase inhibitors.

Related Articles
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