COVER SHEET

TITLE: Exploration of the Relationship Between GRAIL and Cbl-b

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ABSTRACT

Exploration of the Relationship Between GRAIL and Cbl-b

The E3 ligases GRAIL and Cbl-b are necessary for the induction CD4+ T cell anergy. Using CD4+ T cells from wildtype (WT) and Cbl-b knockout (Cbl-$b^{-/-}$) mice, we investigated the relationship between GRAIL and Cbl-b. Induction of anergy led to an 8-fold increase in GRAIL mRNA expression in WT T cells compared to the Cbl-$b^{-/-}$ T cells. In contrast, ectopic expression of GRAIL in WT and Cbl-$b^{-/-}$ CD4+ T cells led to a 30% decrease in proliferation in both groups relative to their respective GFP-transduced control, providing evidence that GRAIL functions independently of Cbl-b for conveyance of an anergic phenotype. In sum, these data suggest a Cbl-b dependent role for optimal upregulation of GRAIL mRNA under anergizing conditions and a Cbl-b independent functional role for GRAIL in the anergic phenotype.

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