

Regulation of T Cell Activation by TIM-1

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Atopic, or allergic, diseases like asthma are marked by a propensity to develop Th2 type T cell responses to environmental antigens, but many questions remain about the molecular basis for this. Transmembrane proteins of the T cell immunoglobulin and mucin domain (TIM) family have recently been implicated in the control of helper T cell-dependent immunity. TIM-1 in particular is an attractive target for study, since it may provide a link to the inverse correlation between hepatitis A virus infection and asthma. Until now, there has been essentially no information regarding the activation of downstream signal transduction pathways by TIM proteins. We have found that TIM-1 can induce signaling pathways that lead to AP-1- and NFAT-dependent transcription in T cell lines. TIM-1 can also augment activation of these pathways by the TCR, suggesting that it functions in a co-stimulatory fashion to increase the efficiency of T cell activation. We also demonstrate that proximal components of TCR signaling are required for TIM-1-dependent signal transduction. These studies provide the first characterization of signaling pathways used by a member of the TIM family, which should lead to a greater understanding of the impact of these molecules on T cell activation and differentiation.