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TIM-1, a novel allergy and asthma susceptibility gene.

McIntire JJ, Umetsu DT, DeKruyff RH.

Division of Allergy and Immunology, Department of Pediatrics, Stanford University, CA 94305-5208, USA.

Abstract

Atopic diseases, including asthma, allergic rhinitis, and atopic dermatitis, are caused by environmental factors in genetically predisposed individuals. Although the prevalence of these diseases has risen dramatically over the past two decades, it has been difficult to identify the underlying causes of these diseases due to the complex interplay between the genetic and environmental factors involved. Using a congenic mouse model of asthma, we simplified this complex trait and identified the novel T cell immunoglobulin domain, mucin-like domain (TIM) gene family, that encodes transmembrane proteins expressed by CD4 T cells. Recent studies demonstrate that the TIM family, particularly TIM-1, plays a critical role in immune responses that regulate the development of atopic diseases. In humans, certain polymorphic variants of TIM-1 are strongly associated with protection against atopy, and this association occurs only in individuals who have had past infection with hepatitis A virus (HAV). Since TIM-1 functions as the cellular receptor for HAV, activation of T cells through TIM-1 by HAV or by its natural ligand may affect T cell differentiation and the development of Th2-driven allergic inflammatory responses. Epidemiologically, HAV infection is associated with a reduced risk of developing atopy, and because the incidence of HAV infection has been significantly reduced in industrialized countries over the past 30 years, the discovery of a genetic interaction between HAV and TIM-1 provides the first molecular genetic evidence for the hygiene hypothesis.

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