Reduced expression of transforming growth factor beta 1 exacerbates pathology in an experimental asthma model.

Abstract:
Allergic asthma is characterized by airway hyperreactivity (AHR), eosinophilic airway inflammation and elevated serum IgE levels. T-helper 2 (Th2) cells play a critical role in the pathogenesis of asthma, but the immunological mechanisms that inhibit Th2 cell function in vivo are not well understood. Conflicting results regarding the protective role of Th1 cytokines and TGF-beta in asthma have been reported. To further investigate the role of TGF-beta(1) in asthma, we examined mice heterozygous for deletion of the TGF-beta(1) gene (TGF-beta(1) (+/-) mice) in a murine asthma model. While TGF-beta(1) (+/-) mice seem phenotypically normal, they express only about 30% of wild type TGF-beta(1) protein levels as shown before. The reduced expression of TGF-beta(1) is accompanied by a strikingly increased eosinophilic inflammation and mucus secretion in response to ovalbumin (OVA) sensitization. Moreover, TGF-beta(1) (+/-) mice develop significantly enhanced Th2-cytokine levels, decreased IFN-gamma production and increased levels of OVA-specific IgE in serum. In contrast, AHR in response to methacholine is not altered significantly. Our data demonstrate that reduced expression of TGF-beta(1) exacerbates pathology in an experimental asthma model and support the view that the elevated levels of TGF-beta(1) in asthmatic airways might be, at least in part, a result of anti-inflammatory
compensation by this cytokine.