Interleukin-4 is involved in allergen-induced airway eosinophilic inflammation and bronchial hyperresponsiveness independent of genetic background

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The role of interleukin (IL)-4 in the development of allergen-induced airway inflammation and bronchial hyperresponsiveness (BHR) is still controversial. To investigate the role of IL-4 in the development of antigen-induced airway inflammation and BHR, we used two different inbred IL-4 gene-knockout mice; one was BALB/c, which is known to be a high IgE responder, and the other was C57BL/6, known to be a low IgE responder and a lower responder to acetylcholine (ACh) in the airways. Mice were immunized with antigen at intervals of 12 days. Starting 10 days after the second immunization, mice were exposed to antigen three times every fourth day. Twenty-four hours after the last antigen challenge, bronchial responsiveness to ACh was measured and bronchoalveolar lavage was performed. In sensitized BALB/c mice, repeated aeroallergen challenge induced dramatic eosinophilia in the airways and severe increases in bronchial responsiveness to intravenous ACh, along with increases in serum antigen-specific IgE. In contrast, immunized C57BL/6 mice, after antigen provocation, developed a minor influx of eosinophils into the airways and only moderate increases in bronchial responsiveness without antigen-specific IgE in serum, indicating that the genetic background influenced not only IgE synthesis, but also the degree of airway inflammation and BHR. Moreover, disruption of the IL-4 gene in both strains of mice abolished allergen-induced BHR, airway eosinophilia and IgE response. Together, these findings suggest that the differences in genetic background can directly influence the pathophysiology of bronchial asthma, including the role of IgE, and that IL-4 has a crucial role in the development of allergen-induced BHR independent of genetic background.

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