

Mechanisms of mucosal inflammation in the nose and lungs

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Asthma and rhinitis are currently considered and defined as a chronic inflammatory disorders of the airway mucosa (1). The pathogenesis of both allergic diseases involves 2 major steps (2). The first step is sensitization to an aeroallergen, leading to the preferential development of Th2 like lymphocytes. The second step occurs only in some individuals and is characterized by the development of a chronic allergic inflammation of the airway mucosa. This inflammatory process, which is thought to be largely Th2 cell driven, involves a variety of cells and mediators and appears to be orchestrated and regulated by a highly complex network of mutually interacting cytokines. Biopsy studies in asthma illustrate increased expression of Th2 like cytokines such as IL-4, IL-5 and IL-13, proinflammatory cytokines including TNF α and IL-1 β and chemokines such as IL-8, MCP-1 and RANTES. The expression of growth factors such as TGF β , PDGF, IGF and EGF remains somewhat debated at present (3-7).

Although our understanding of the pathophysiology of asthma has evolved substantially over the past years, a number of issues remain to be clarified. This includes an even better understanding of the sensitization process, leading to a preferential Th2 cell development, and the precise functional importance of each cell and mediator in the intricate relationship between inflammation, remodeling and altered airway behaviour.

Providing proof of the functional importance of a given mediator in a disease process usually follows Koch's postulates. Applying these to the role of a given cytokine in asthma, this means showing that a cytokine is present in asthmatic airways, that exogenous administration can mimic the effects of allergen exposure and finally that specifically antagonizing the cytokine affects criteria of disease activity in ongoing day to day asthma. So far, for

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obvious ethical reasons, experiments in man have been restricted to a morphological analysis together with a few studies that have examined the effect of inhaling cytokines on airway function (8, 9). The development of specific and potent cytokine antagonists that can safely be used in man is eagerly awaited. In the meantime however, interesting data emerge from in vivo animal models of allergen induced airway changes, in particular from the gene knock-out models of asthma that have been developed over the past few years in mice (10). The majority of these models has evaluated the exact functional role of Th₂ cells, IL-4, IL-5 and IgE in the pathogenesis of allergic airway inflammation

and airway hyperresponsiveness. From these experiments, the central role of T cells clearly emerges. It would also appear that IL-5 is indeed essential for the development of airway eosinophilia. However, these experiments also show that neither the IL-5/eosinophil axis nor the IgE/mast cell axis are the cause of allergen induced airway hyperresponsiveness. Indeed, it clearly emerges from various experiments that the T-cell in its own right is the main determining factor in establishing the degree of airway hyperresponsiveness, probably through the release of a mix of cytokines, the composition of which can vary depending on the stimulus used (11–16).

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