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Suppression of immediate and late cellular and functional responses to antigen by a non-anaphylactogenic anti-IgE antibody in a murine model of asthma

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Eosinophils are present in the human and animal airways during allergic reactions, but animal models have shown that their presence is not sufficient for the development of bronchopulmonary hyperreactivity (BHR). Indeed, intense eosinophilia can be induced by antigenic challenges, in the absence of BHR. Other factors seem to be required. Using the BP2 mice (Bons Producteurs) selected for the production of large amounts of antibodies, we developed a procedure in which single antigenic provocation leads to intense mucosal and submucosal eosinophil infiltration, with BHR starting by one hour and lasting at least 6 days. CD4+ lymphocytes, a potential source of IL-4 and IL-5, two cytokines of allergy which are produced by Th2 lymphocytes, were present in the airways mucosa and bronchoalveolar lavage fluid, together with eosinophils. TNF-α. Was identified by 1-2 hours and IL-4 and IL-5 by 24 hours. Most interestingly, from 48 hours on after the antigenic provocation, an intense mucosal metaplasia was observed and most, if not all, of the Clara cells contained mucosal granules in abundance.

This convenient model in which a single antigenic provocation induces what usually requires multiple provocations in other strains of mice, was used for drug studies. Thus dexamethasone, a model steroid, was efficient at the 0.5 - 2.0 mg kg^{-1} range in suppressing all the tested parameters. A monoclonal non-anaphylactogenic rat anti-mouse IgE (mAb1-5), given within 24 h before challenge with antigen, reduced tissue eosinophilia, mucous metaplasia, and bronchopulmonary hyperreactivity as well as IL-4 titres in the bronchoalveolar lavage fluid. Kinetic studies suggested that inhibition by mAb1-5 may result from competitive displacement of IgE from its receptors, thus preventing cell stimulation, and not simply from the exhaustion of circulating antibodies. Thus, both IgE and eosinophils play an essential role in the early and delayed expression of airways inflammation and the accompanying BHR in a murine model of asthma. This model is particularly convenient for mechanistic and pharmacological studies.