

Allergic Respiratory Responses to Der p 1 in Mice

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Clinical models of human allergic diseases are particularly useful to assist in the understanding of the mechanism of primary sensitisation and the early immunopathogenic inflammatory events. Immunisation of animals by the respiratory route can in either tolerance [1] or sensitisation [2] depending in part on dosage and choice of adjuvant. Recent human studies have shown interesting data concerning bronchial and interstitial distribution of inflammatory activity, although these studies were done on long-standing asthmatics [3, 4]. Allergens from the house dust mite (HDM) have been shown to be important in the development of allergic respiratory disease with up to 80% of Australian asthmatics sensitive to HDM versus 10% of controls. In this study we have used the purified major HDM allergen Der p 1 and investigated allergen-specific T-cell responses in draining lymph nodes and spleen, specific IgE production and pulmonary histologic changes following respiratory immunisation.

High-responder C57BL/6 mice were immunised subcutaneously with Der p 1 (0.1–50 µg) in alum. Mice were bled and boosted 14 days later with Der p 1 intranasally. Mice were killed on day 17, and the spleen and superficial cervical lymph nodes were removed for cell culture. Lungs were fixed in situ with formalin and removed for histologic analysis. Der-p-1-specific IgE titers before and after boosting were determined by PCA and T-cell reactivity was as-

sessed using the FDC-P1 bioassay for IL-3/GM-CSF production. Lung sections were stained with haematoxylin-eosin and the cellular infiltrate was quantified by image analysis. The total inflammatory percentage of the lung was determined and the number of eosinophils in the alveolus, the alveolar wall and peribronchial eosinophils surrounding bronchi and bronchioles were counted.

Strong T-cell responses, measured by IL-3/GM-CSF production, were evident in the spleen and draining lymph nodes following subcutaneous immunisation with Der p 1. Intranasal boosting with Der p 1 reduced the magnitude of these responses, especially in the spleen. Immunisation of mice subcutaneously with alum and Der p 1 followed by intranasal boosting led to a substantial inflammatory infiltrate in the airways and alveolar regions of mouse lungs. In unboosted mice, only minimal infiltrate was evident. Using objective measures of inflammatory infiltrate, the intranasal boosting augmented the extent and severity of allergic inflammation. In mice with severer inflammatory changes, eosinophilic aggregates, Charcot-Leyden crystals and mucus were evident. At the time point studied, subcutaneous priming (of Der p 1 with alum) without boosting did not result in a substantial increase in alveolar wall or space eosinophil numbers. Significant differences were observed in eosinophils numbers in both alveolar sites, wall $p = 0.01$ and space $p = 0.012$. In some groups of mice, priming plus intranasal boosting led to an increase in alveolar inflammation. Mice which were boosted also showed increasing numbers of peribronchial eosinophils with increasing intranasal boosting dose and no significant peribronchial eosinophil infiltrates were evident in mice that received on-

ly priming or boosting. The airway diameter was highly inversely correlated with the number of eosinophils per millimetre length of basement membrane ($p = 0.001$), i.e. smaller airways had substantially greater eosinophilic infiltrates.

In conclusion, we described a murine model of allergy to the house dust mite exhibiting many of the histologic features of human asthma, in the presence of allergen-specific cellular and serologic reactivity.

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