Allergen vaccines: major or multi allergen-directed strategies?

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Inflammation in the airways of asthmatics results from immune responses to complex sources of allergens such as cats and house dust mites. The current practice of immunotherapy with extracts of allergens shows that modifying the immune response can ultimately treat allergic disease but that new strategies are required to achieve faster responses with less trauma. It is likely that the new strategies for accomplishing this, such as the use of peptides, recombinant allergens and adjuvanted conjugates will use molecularly-defined formulations. A key question therefore is whether or not effective treatment can be achieved with just the dominant allergens. It is equally important to assess whether or not the current therapy with extracts targets a large number of specificities or just responses to the few allergens present in high concentrations. This could indicate an alternative strategy for better immunotherapy with formulations in which the important allergens and possibly regulatory specificities are all present in balanced and effective concentrations. The results of clinical trials with defined major allergens for ragweed, grass, birch, bee venom and cat will be analysed in relation to the known complexity of the sources of allergen. This will include the description of newly recognised allergens of cat, including lipocalin, haptoglobin and S 100 A 12. The spectrum of house dust mite allergens will be analysed in more detail to assess the association of IgE binding activity and the production of effector (IL-5, IL-13) and regulatory (IFN-γ, IL-10) cytokines. To date it appears that the major specificities Der p 1 and Der p 2 are the dominant inducers of both regulatory and allergenic responses. Study of the contribution of high molecular weight allergens is however emergent and their allergenicity may be underestimated. Progress on the characterisation of the paramysoin, chitinases and the vitelligenin-like M-177 allergen will be presented. Absorption experiments with recombinant allergens also show that a further low molecular allergen, possibly Der p 12, makes a hitherto unappreciated contribution to IgE binding. The results of studies in different populations also show that allergen recognition varies in different geographical regions, as documented for tropomyosin, and this could have implications for both treatment and diagnosis. It thus appears that the major allergens Der p 1 and Der p 2 are reasonable targets for new strategies of immunotherapy but that responses to other allergens need to be elucidated. Recent studies on the ability of different allergens to induce the production of the regulatory T-cell transcription factor FoxP 3 however show that minor house dust mite allergens can induce similar responses to the major allergens. There is thus the potential for these allergens to induce regulatory effects during immunotherapy. Bystander effects in which one antigen can regulate responses to other allergens have been frequently documented, but although experiments with regulatory cells imply that epitope spreading is part of their action, this yet to be demonstrated. Another mechanism that will be described is deviation where tolerisation of Th 2 responses produces a milieu for the development of Th 1 type immunity.