Unique Immunotherapy approaches: Allergoids

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Polymerization with glutaraldehyde is a modification procedure of allergen extracts that has been extensively studied for the production of high molecular weight allergoids. With this process, IgE-binding epitopes are hidden within a complex macromolecular network, which leaves most of the antigenic determinants accessible for the induction of IgG antibodies. T cell epitopes are left untouched for T cell recognition[1],[2],[3],[4],[5]. Therefore, glutaraldehyde-modified therapeutic allergic vaccines are safer than unmodified vaccines, while retaining clinical efficacy.

Glutaradehyde modified allergens (Polymers) are processed in a different way than intact allergen molecules. Native allergens can degranulate mast cells and basophils and utilize an IgE-mediated antigen presentation, which leads to increased Th2 cytokine and IgE production. In contrast, modified allergens lacking IgE-binding sites utilize phagocytic or pinocytic antigen-uptake mechanisms by dendritic cells and monocytes/macrophages, generating a balanced Th0/Th1-like cytokine pattern by T cells, and resulting in normalized isotype production by memory B cells.

We have recently demonstrated that the allergen uptake by monocyte derived dendritic cells is significantly greater when the allergen (*Dactylis glomerata*) is a polymer than when it is in its native form. Additionally, the polymer is able to differentiate these cells better than the native extracts.

Immunotherapy is safe and effective to treat allergic respiratory diseases produced by the inhalation of grass pollen allergens[6],[7]. Cluster immunotherapy is increasingly being used as a

safe and effective method of immunotherapy. It allows for a rapid and safe build up phase, reaching maintenance in just a few injections. It was first described by Norman et al.[8] using the recently developed allergoids. Although it has also been successfully explored with native allergens[9],[10],[11], the commercial availability of allergoids in Europe is considered the most important reason for the increased use of cluster immunotherapy. It has been proposed, that immunotherapy with allergoids allows the administration of higher doses of allergen[12],[13] and, therefore, clinical effects of immunotherapy with allergoids may start earlier than with conventional immunotherapy.

Several studies have been published using grass allergoids for subcutaneous immunotherapy and showing various degrees of efficacy. The comparison of these studies is difficult since the use of formaldehyde[14],[15],[16],[17],[18],[19],[20],[21], or glutaraldehyde[22],[23],[24],[25] produces allergoids with different characteristics. Other important differences are the lengths of the studies, the doses given, the administration schedules and the ways in which efficacy was assessed. While some studies have used rush, or cluster protocols and evaluated safety, others have used more traditional build-up schemes and evaluated efficacy using different parameters. Preseasonal immunotherapy schedules usually use a cluster immunotherapy protocol, which consists of the grouped administration of 2 or more doses of immunotherapy in one day. Maintenance can be reached within 1 to 2 weeks.

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