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Mechanisms of allergen immunotherapy

Allergen immunotherapy is allergen specific, allergen dose- and time-dependent and induces long lasting tolerance that persists for years after discontinuation. Successful immunotherapy is accompanied by suppression of allergic inflammation in target organs and increases in 'protective' non-inflammatory blocking antibodies of the IgG (particularly IgG4) and IgA2 subclasses with inhibitory properties[1].

These events are accompanied by a reduction and/or redirection of underlying antigen specific Th2-type T-cell-driven hypersensitivity to the allergen(s) used for therapy. This suppression occurs within weeks or months as a consequence of the appearance of a population of regulatory T-cells that exert their effects by mechanisms involving cell-cell contact, but also by release of factors such as interleukin 10 (IL-10) (increases IgG4) and TGF-beta (increases specific IgA)[2]. The more delayed-in-time appearance of antigen specific Th1 responses and alternative mechanisms such as Th2 cell anergy and/or apoptosis of antigen specific cells may also be involved.

Sublingual immunotherapy has also been shown to induce long-term tolerance with remission for at least 2 years following a 3-year course of treatment[3]. The mechanisms of sublingual immunotherapy are similar to those following subcutaneous administration of allergen, whereas it is likely that additional events following antigen presentation in the sublingual mucosa and regional lymph nodes are also involved.

These mechanistic insights have resulted in novel approaches and portend future biomarkers that may be surrogate or predictive of the clinical response to treatment.

References

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