



***In vitro allergen-induced RNA expression of signaling lymphocytic activation molecule by PBMC of patients with allergic rhinitis is increased during specific pollen immunotherapy.***  
**Laaksonen K, Junikka M, Lahesmaa R et al. *J Allergy Clin Immunol* 2003; 112 (6): 1171-1177.**



## The synthesis of SLAM may be the making of immunotherapy

With specific immunotherapy the desired outcome is a switch from T-helper cell activity concerned with allergy to those T-helper cells concerned with cell mediated immunity – the switch from T<sub>H</sub>2 to T<sub>H</sub>1 activity. A well-known marker for T<sub>H</sub>1 activity is Signalling Lymphocytic Activation Molecule (SLAM). SLAM is a transmembrane lymphocytic receptor that gets rapidly up-regulated following cell activation. It is associated with T cell proliferation and the synthesis of interferon gamma (IFN- $\gamma$  and interleukin 10 or IL-10). Raised levels of SLAM, IFN and IL are seen in patients with autoimmune disease but little is known about the significance of SLAM in specific immunotherapy aimed at treating allergic patients. A team in Finland have now demonstrated that SLAM synthesis is a key factor in the reduction of allergic symptoms and the success of immunotherapy. To measure SLAM, the team assayed the mRNA required for SLAM synthesis in

mononuclear cells found in peripheral blood (PBMCs). In patients with allergic rhinitis there was less SLAM mRNA than in healthy controls. After one year of specific immunotherapy (SIT) for the treatment of birch (*Betula verrucosa*) allergy, there is more SLAM mRNA activity in treated patients than in untreated patients. Furthermore, those patients treated successfully with SIT (better symptomatic improvement) showed an early rise in SLAM synthesis followed with a drop after one year. Patients who had less symptomatic improvement showed a more gradual increase in SLAM synthesis over the year. Although limited to PBMC and not the mononuclear cells and dendritic cells found in tissue, this research suggests that SLAM is involved in the T<sub>H</sub>2 to T<sub>H</sub>1 switch. The researchers suggest that T<sub>H</sub>1 cell activation by SLAM and the resulting production of IFN- $\gamma$  in SIT.

***Effects on inflammation parameters of a double blind, placebo controlled one-year course of SLIT in children monosensitized to mites.***  
**Marcucci F, Sensi L, Frati F et al. *Allergy* 2003; 58: 657-662.**



## Biochemical markers of successful SLIT in childhood dust mite allergy

A double blind, placebo controlled trial has shown that sublingual immunotherapy (SLIT) can prevent nasal tryptase secretion and nasal IgE specific to dust mite allergens in children sensitised to dust mites. Whereas most studies look at clinical scores when assessing efficacy, few have considered immunological and inflammatory parameters. Furthermore, a lack of clinical studies in children may explain why there is no official guidance on the use of sublingual therapy for the treatment of children allergic to perennial allergens. Researchers in Italy examined twenty-four children between the ages of 4 and 16 years who were monosensitized to dust mites and randomised to receive SLIT or placebo over a twelve-month study period. In children receiving SLIT, there was a decrease in nasal eosinophil chemotactic protein (ECP) and a slight increase in sputum ECP. In the placebo group, there was a rise in nasal ECP and a sharp increase in sputum ECP. In the SLIT group, there was a significant decrease in sputum tryptase and an insignificant change in nasal tryptase. In the

placebo group, sputum tryptase was unchanged and nasal tryptase levels were significantly raised. There was a statistically significant rise in nasal mite-specific IgE in the placebo group but no significant difference between groups for serum or nasal IgE. However, the symptom scores for treated patients were significantly improved compared with those for untreated children. Although this study did not aim to assess the safety of SLIT in children with perennial allergy, the authors concluded that the use of SLIT for the treatment of a perennial condition was equivalent to their previous studies. However, they consider that inflammation due to perennial allergy needs to be assessed over a longer period than inflammation due to seasonal allergy. Long-term studies have shown that SLIT has beneficial results in perennial allergic conditions where short-term studies have not. The authors define long-term treatment as 18 months or more and they are therefore extending their study to see what differences will arise.

**Safety of rush insect venom immunotherapy. The results of a retrospective study in 178 patients.**  
**Wenzel J, Meissner-Kraemer M, Bauer R et al. Allergy 2003; 58: 1176-1179.**



## New protocol for venom immunotherapy

A team from the University of Bonn has developed a modified immunotherapy protocol for desensitising patients allergic to insect venom.

Their rush venom immunotherapy (VIT) protocol involves daily injections of venom preparations of increasing concentration from Monday to Friday, when the maximum dosage of 100 mg/ml is reached. Following a weekend break, two further maximum doses are given. In a retrospective analysis of 178 patients treated this way, it was found that the greatest risk of systemic reactions occurred on day five but the risk then dramatically fell after the weekend, despite the same maximum dose being administered on the following Monday and Tuesday.

The team speculate that the weekend break is a likely explanation for the relatively low incidence of systemic events they have encountered. Up to 5% of Europeans have

a history of generalised skin or systemic reactions to insect venom.

Honeybees and wasps are common culprits and occupations such as beekeeping, forestry or handling cakes and pastry put sensitised patients at risk.

Conventional immunotherapy aimed at hyposensitisation takes several weeks. Rush VIT takes 5 to 7 days and ultra rush only 1 to 3 days but these protocols produce an incidence of systemic side-effects of between 20 and 45% – the authors of the Bonn findings emphasise the need for a universal measure of scoring systemic reactions and propose the Mueller I-IV score.

The “Bonn rush VIT protocol” takes seven days with a possibly crucial two-day holiday between day 5<sup>th</sup> and 6<sup>th</sup> days of treatment. As a result, the incidence of systemic reactions is only 17.9%. Happy weekend!

**Inhibition of allergen-IgE binding to B cells by IgG antibodies after grass pollen immunotherapy.**  
**Wachholz PA, Kristensen Soni N, Till SJ, Durham SR. J Allergy Clin Immunol 2003; 112: 915-922.**



## Allergen-specific IgG stops B cells becoming allergen presenters

The progression from allergen exposure to IgE production is quite well understood with B cells and other antigen-presenting cells playing a key role. Although immunotherapy (IT) has been shown to produce a reduction in IgE antibodies, the clinical relevance and role of IgG as a “blocking antibody” is less certain. For example the level of IgG induction does not always correlate with the level of protection conferred by IT, especially against wasp and bee stings.

Now researchers from the United Kingdom and Denmark have developed a cytometric assay that reveals the degree of binding between specific allergen-IgE complexes and the low affinity IgE receptor on B cells known as CD23. In patients with hayfever, subcutaneous immunotherapy, but not placebo treatment, was associated with reduced allergen-IgE binding to B cells and this was due to the induction of allergen specific IgG. Grass pollen specific IgG had no effect on birch allergen-IgE binding to B cells.

The assay showed that allergen-specific IgG does not bind to

B cells to prevent allergen-IgE binding but prevents the formation of complexes themselves. In the presence of a low allergen concentration, IgE molecules form large complexes containing IgE and allergen.

At higher concentrations of allergen the complexes are smaller, consisting of individual antibodies with few unoccupied sites. Allergen-specific IgG effectively displaces IgE from these complexes and is particularly effective at low allergen concentrations. The authors suggest that IT changes the character of allergen-specific IgG as well as increasing its quantity. Their assay measures the functional activity of IgG and is therefore a better measure of IT than merely measuring serum concentration. Furthermore, the assay obviates the need for expensive and time-consuming culturing of T cells that has been required for assessing antigen presentation.

The mechanism for other APCs demands investigation and one of the biggest questions remaining is: how does IT induce the formation of blocking IgG antibodies?