

The role of peanut-specific T cell responses in children with and without peanut allergy

Maes o ddiddordeb ymchwil: [Food hypersensitivity](#)

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Background

Peanut allergy is a severe, potentially life-threatening condition in children characterised by severe anaphylactic reactions triggered by even minute quantities of peanut allergen. It remains unclear why some children develop peanut allergy, others tolerate peanut their whole lives and other children outgrow their peanut allergy to subsequently develop tolerance. It is equally unclear why some children have evidence of specific IgE to peanut or a positive skin prick test to peanut and nevertheless eat large quantities of peanut without ill effect. In our previous funded work, clinical and immunological observations relating to the different states of peanut allergy and tolerance have been made. This study enabled us to further understand T cell responses in the pathogenesis of food allergy by understanding the mechanisms that underlie T cell responses in tolerant individuals and devise new immunomodulatory strategies that could allow us to normalise T cell responses in future therapies.

Research Approach

In the first stage of this study, a recently developed method was used to explain the differences in the mechanism of T cell responses in children with peanut allergy (PA), tolerant children (NA) and outgrowers (OG). In particular, differences in memory versus naive T cell responses and allergy specific T cell precursor frequency will be investigated. Also to be investigated was the role of suppressor T cells and whether IgE mediated facilitated antigen presentation (FAP) can explain the observed differences.

In the second stage of the study, observations on T cell responses were extended to include children with peanut sensitisation who were able to tolerate peanut. This was so that clinical differences between peanut allergic and peanut sensitised individuals could be established.

The third stage of the study investigated the site (via the skin or gut) where sensitization to peanut has occurred in peanut allergic individuals.

Memory T cells express 'homing receptors' on their surface that assist the circulation of the T cell through lymph nodes, lymphatics and the blood before returning to the tissue where the T cell is most likely to encounter the allergen again. The researchers will investigate two specific homing receptors - the Cutaneous Lymphocyte-associated antigen (CLA) - a skin homing receptor, the expression of which implies sensitization in the skin and $\alpha 4 \beta 7$ integrin - a gut homing receptor, the expression of which implies sensitization in the gut. These studies compared the proliferative

T cell responses to peanut in peanut allergic children amongst the CLA-expressing (skin homing) and $\alpha 4\beta 7$ integrin-expressing (gut homing) T cell populations.

Results

A significant difference was observed in peanut-specific T cell responses between children with peanut allergy (PA) and children tolerant to peanuts (NA). The researchers undertook experiments to investigate four possible explanations for these differences and determined that the differences were most likely explained by the presence of peanut-specific IgE facilitating antigen presentation (FAP) in peanut allergic children thereby maintaining the allergic response. This mechanism could explain why extremely low levels of peanut proteins that may not trigger allergic reactions could nevertheless be sufficient to maintain peanut allergic responses.

In both peanut allergic (PA) and tolerant to peanut (NA) children, peanut specific responses were found to be driven by memory Th cells and not by naïve T cells. The researchers could not find any obvious differences between the levels of suppressor cytokines produced in peanut-specific responses by peanut allergic (PA) and tolerant to peanut (NA) children. Therefore it seems very unlikely that suppressor cytokines are the cause of the differences between PA and NA states.

In the second stage of the study, the researchers' findings confirmed that B cell responses to allergens (but not those to non-allergenic proteins) are ongoing responses that are closely linked with allergen –specific T cell responses, possibly through the positive feedback mechanism triggered by IgE-mediated facilitated antigen presentation (FAP).

In the third stage of the research, it was found that in peanut allergic (PA) children, the peanut-specific response is predominantly generated by skin-homing CLA⁺ memory T cells that have initially seen peanut antigens in the skin. Peanut-specific responses in children tolerant to peanut (NA) are generated by both skin-homing and gut-homing memory Th cells. It seems that these differences are specific for peanut responses as when carried out with a control food antigen (ovalbumin), no differences were seen between peanut allergic (PA) and tolerant to peanut (NA) children i.e. control responses showed no clear subset predominance of skin-homing or gut-homing memory Th cells.

These results were potentially very significant because they suggest that exposure to peanut allergen through the skin might be the major sensitising route and that interventions aimed at preventing peanut allergy should be focussed on this route of exposure. It is hypothesised that skin exposure to peanuts, presumably through inflamed, eczematous skin may lead to peanut allergy development. New Agency funded research is looking into this further (T07060).

Published Papers

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2. V. Turcanu, A. C. Stephens, S.M.H. Chan, F. Rancé and G. Lack, IgE-mediated facilitated antigen presentation underlies higher immune responses to peanut in allergic individuals compared with tolerant individuals. Manuscript in preparation
3. Chan, S., Turcanu, V., Stephens, A. (2008) In Vitro Evidence For Different Routes Of Sensitization To Peanut In Children. *The Journal of Allergy and Clinical Immunology*. 121 (2) S214. Chan, S., Turcanu, V., Stephens, A., Fox, A., Grieve, A., Lack G. (2012) Cutaneous lymphocyte antigen and $\alpha 4\beta 7$ T-lymphocyte responses are associated with peanut allergy and tolerance in children. *Allergy*, 67 (3): 336–342. Abstracts
4. S.M.H. Chan, V. Turcanu, A.C. Stephens, G. Lack, In Vitro Evidence For Different Routes Of Sensitization To Peanut In Children *J Allergy Clin Immunol* 121: S214, 2008.

5. S. Hingley, G. Du Toit, G. Roberts, V. Turcanu, G. Lack, H. Fisher, and P. Lau, Peanut-specific IgG4 and its association with peanut allergy. J Allergy Clin Immunol 117: S33, 2006.
6. V. Turcanu, A.C. Stephens and G. Lack, IgE-mediated facilitated antigen presentation augments immune responses to peanut antigens in allergic individuals compared with tolerant individuals - The annual meeting of the European Academy of Allergy, Asthma and Clinical Immunology, June 2006
7. V. Turcanu and G. Lack, Levels of peanut-specific precursor T cells reflect peanut allergy status. J Allergy Clin Immunol 115: S62, 2005.

Research report

England, Northern Ireland and Wales

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