

Elucidation of the role of B cells in food allergy, sensitization, and tolerance



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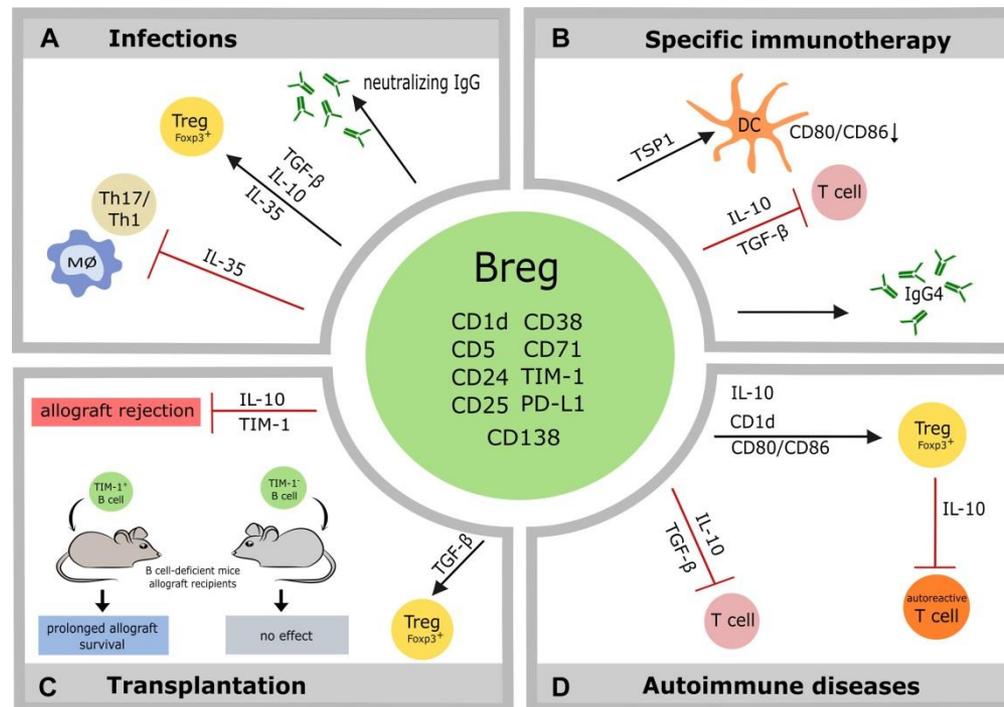
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Allergic tolerance: **IgG4, IL-10**

- **Associated with decreased allergen-specific IgE and increased allergen-specific IgG4**
- **IgG4 may be protective in food allergy**
 - During oral immunotherapy, allergen-specific IgE levels decrease and allergen-specific IgG4 levels increase
 - **IL-10** has been shown to downregulate IL-4-induced production of IgE and upregulate IL-4-induced production of IgG4
 - Cow's milk-specific IgG4 levels increase in children who outgrow cow's milk allergy
 - Sera from children tolerant to peanut block activation of peanut-sensitized mast cells following peanut exposure
 - Effect abrogated if sera depleted of IgG4

Regulatory B cells: IgG4 + IL-10

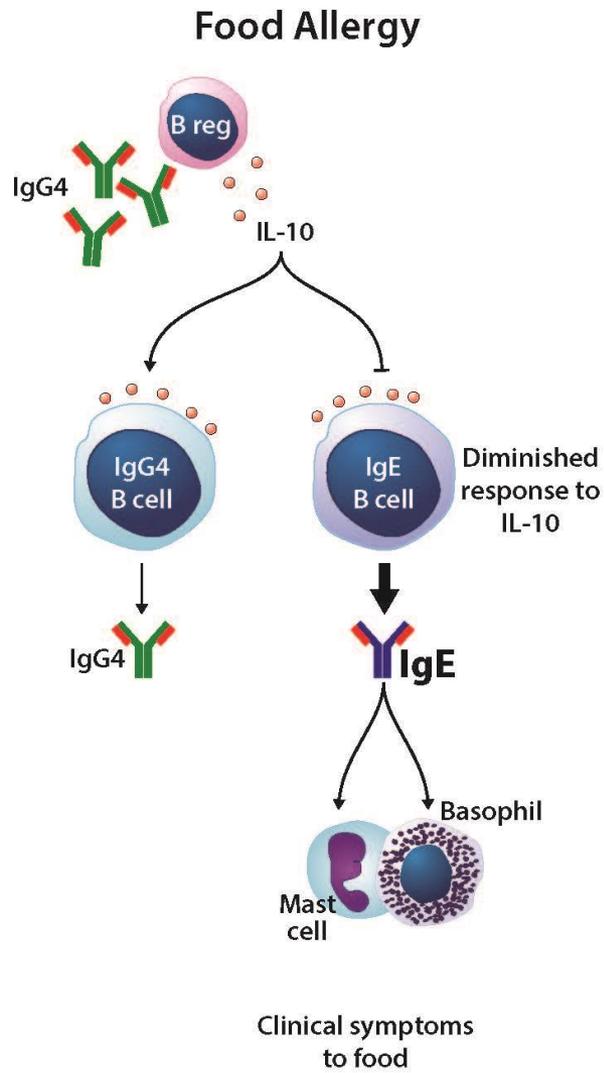
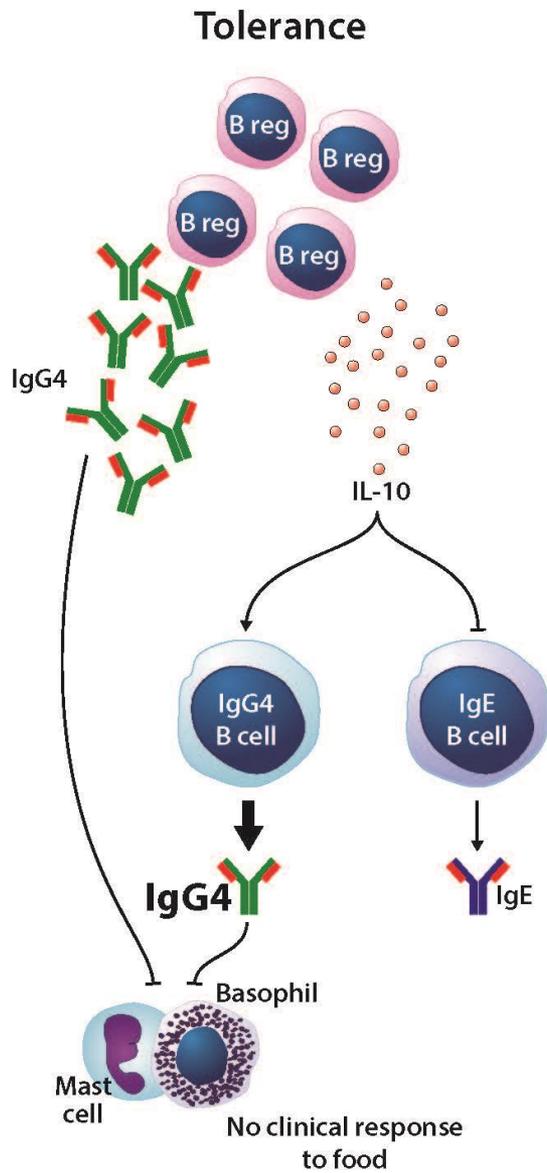
- IL-10-producing B cells produce more IgG4 than non-IL-10-producing B cells
 - CD73- CD25+ CD71+** B cells increased in tolerant beekeepers during beekeeping season and in allergic individuals following IT
- One study has shown that frequencies of regulatory, IL-10+ B cells are lower in food-allergic individuals than non-allergic controls
 - Adults with cow's milk allergy



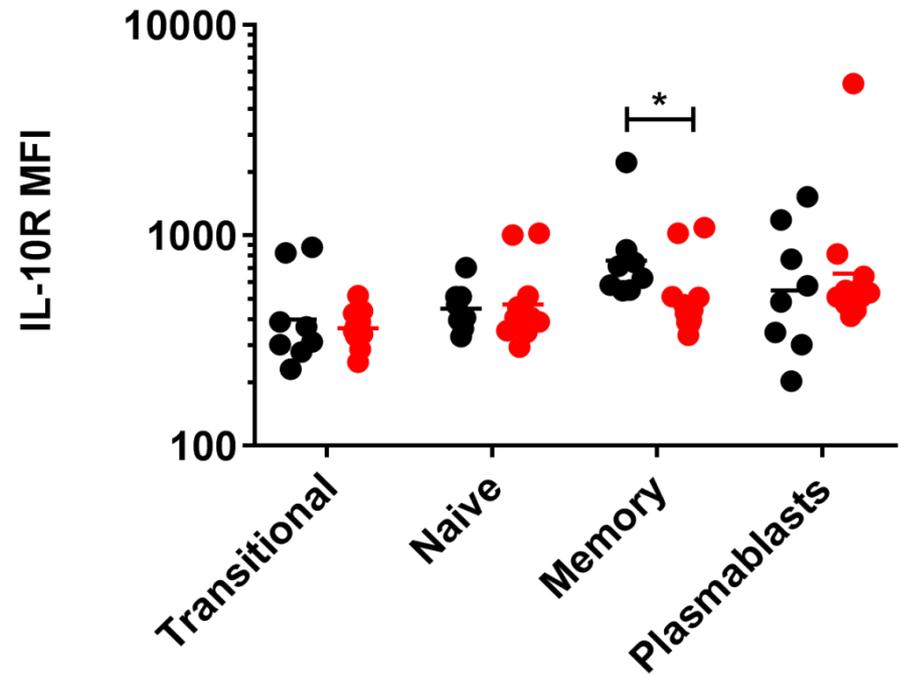
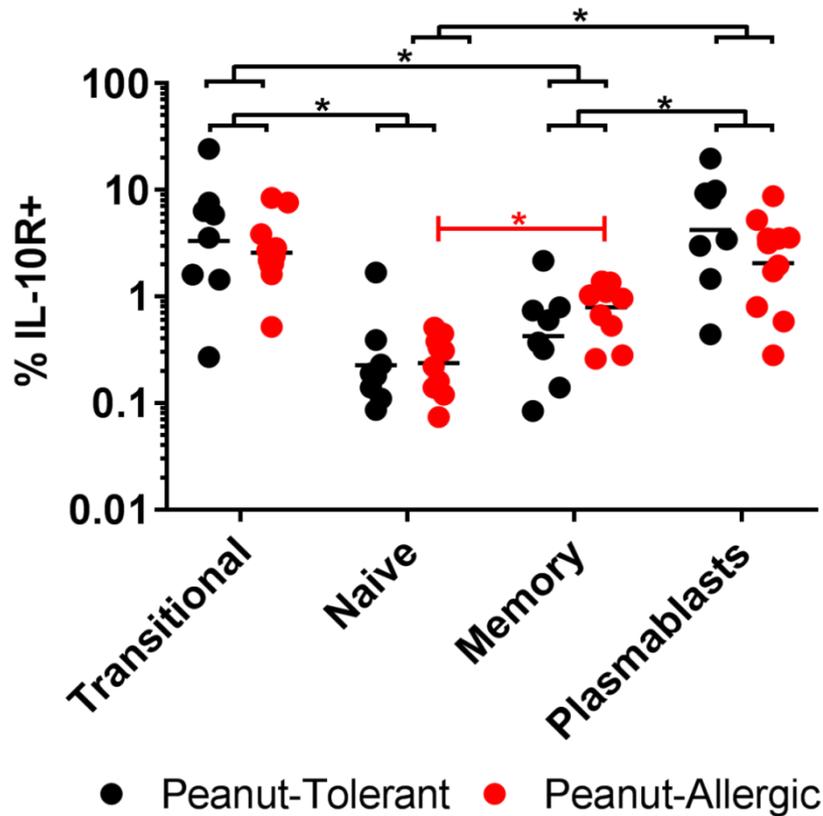
Hypothesis

Decreased B cell responsiveness to IL-10 and decreased Breg frequency and function underlie the development of food allergy

- Examine B cell response to IL-10 and Breg frequency and function in:
 - **Peanut Allergic (PA)**
 - **Peanut Sensitized**
 - **Non-allergic**
- } Peanut Tolerant (PT)



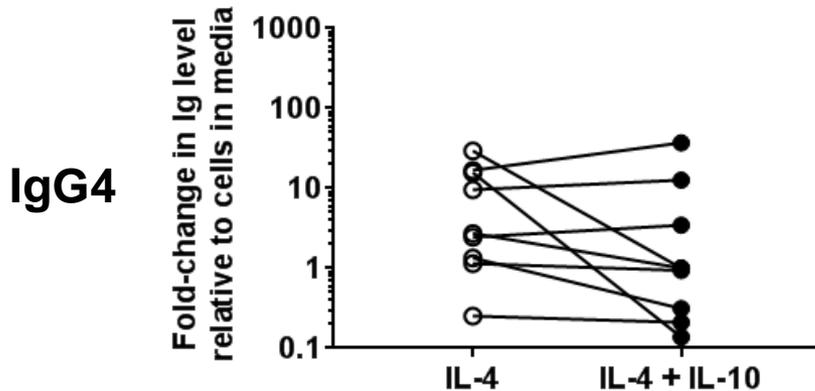
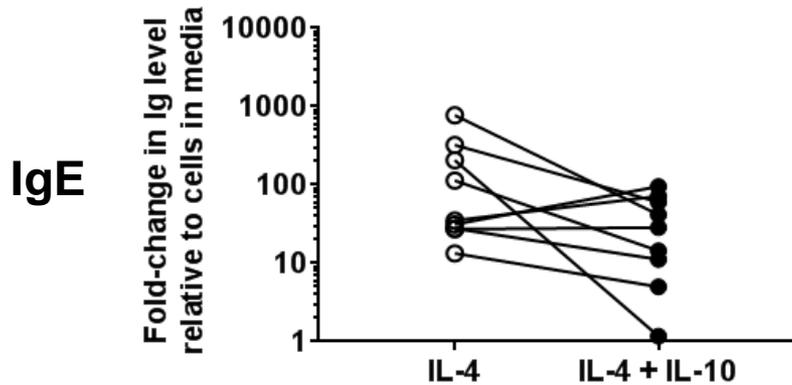
IL-10R expression per cell is increased among memory B cells in peanut-tolerant children



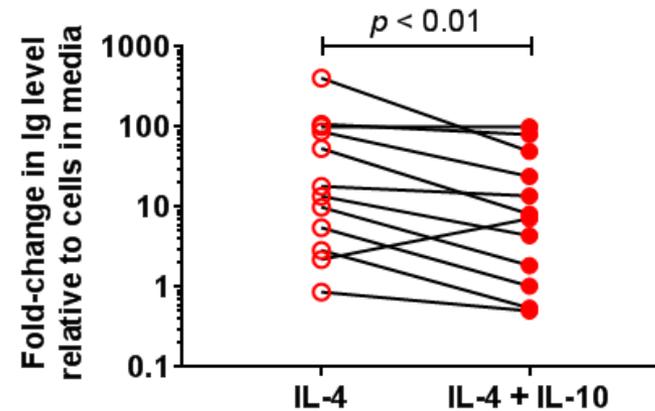
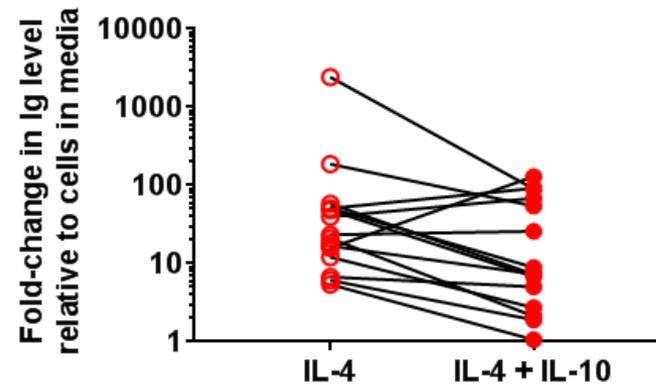
* $p < 0.02$

IL-10 decreases IL-4-induced IgG4 production by PBMCs in peanut-allergic children

Peanut-Tolerant



Peanut-Allergic



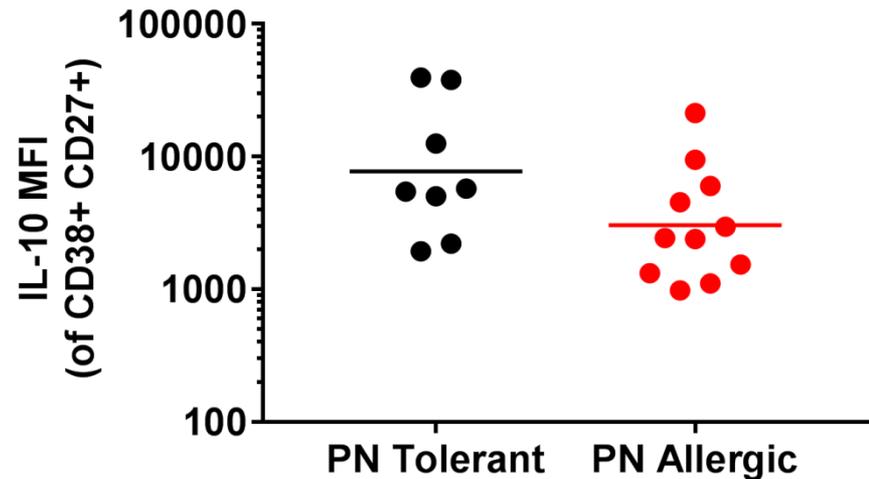
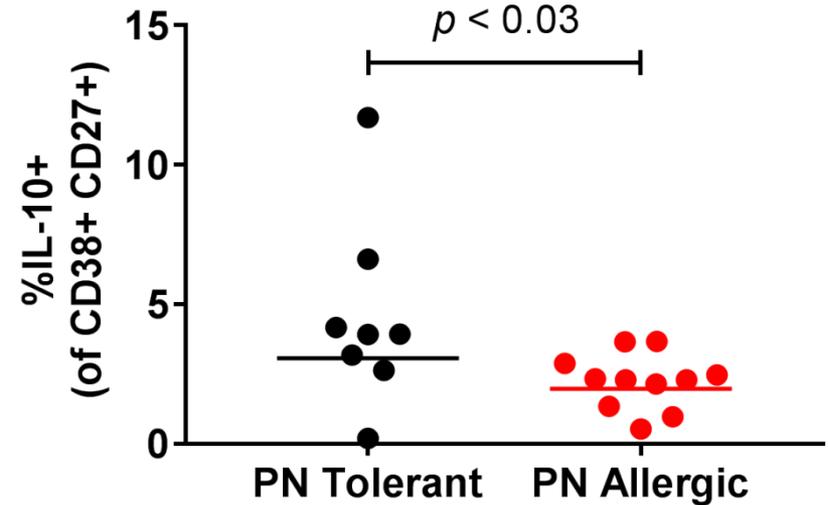
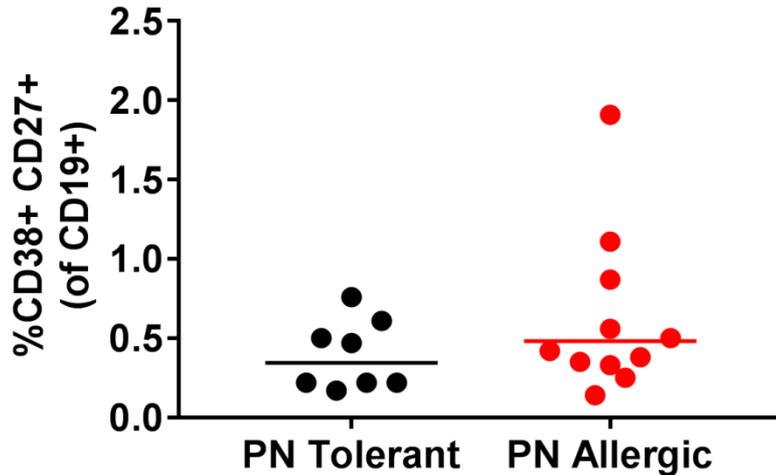
Regulatory B cells (CD19+, IL-10+)

- CD24+ CD27+
- CD24+ CD38+ (transitional)
- CD38+ CD27+ (plasmablasts)
- CD73- CD25+ CD71+ (bee venom immunotherapy)

Regulatory B cells (CD19+, IL-10+)

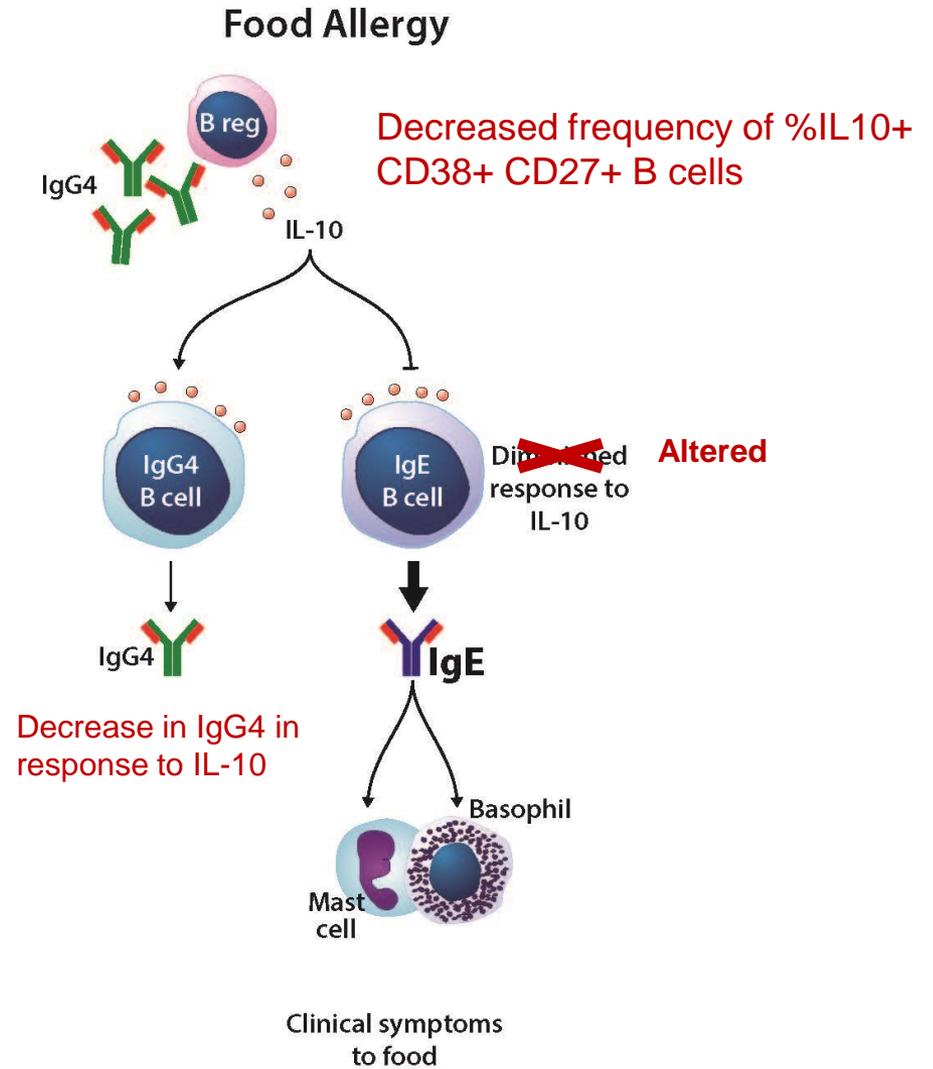
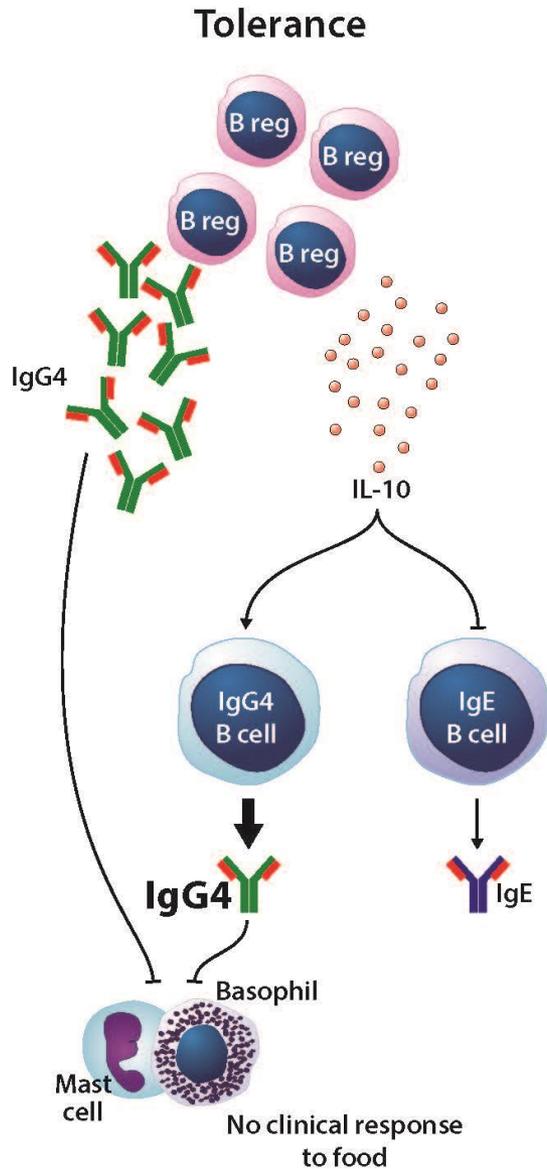
- CD24+ CD27+ I'm not convinced I've actually identified these
- CD24+ CD38+ (transitional) No difference between PT and PA
- CD38+ CD27+ (plasmablasts)
- CD73- CD25+ CD71+ (bee venom immunotherapy)
 - No difference between PT and PA

CD38+ CD27+ (Plasmablast) B regs



Summary

- IL-10R most frequently expressed on plasmablasts and transitional B cells
 - Both peanut-tolerant and peanut-allergic children
 - No difference in IL-10R+ frequency between PT and PA groups
- More IL-10R is expressed per cell on memory B cells in PT children than in PA children
- IL-10 decreases IL-4-induced IgG4 production by PBMCs in PA children
 - IL-10 does not significantly affect IL-4-induced IgE production by PBMCs in PT and PA children
- Different regulatory B cell subsets can be identified in peanut-tolerant and peanut-allergic children
 - Increased frequency of IL-10+ cells among CD38+ CD27+ subset



Future directions/questions

- What is the effect of IL-10 on Ig production in the presence of allergen? Does it differ between allergic and non-allergic children?
 - Stimulation of PBMCs with peanut; addition/inhibition of IL-10
- How do IL-10/B regs affect allergen sensitization and subsequent development of allergy?
 - Blockade of IL-10, inhibition/alteration of B cell differentiation in animal models during allergen sensitization
- Effect of OIT, dupilumab on B regs and IL-10 response



- Catherine Bollard, M.D., M.B.Ch.B.
- Pamela Guerrero, M.D., Ph.D. (NIH)
- Elizabeth Matsui, M.D., M.H.S.
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- CNMC Division of Allergy/Immunology



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How Allergies Work

