Weill Cornell Medicine

Gene Therapy to Prevent Reaction to Allergens

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Gene Therapy to Prevent Reaction to Allergens

Background & Unmet Need

- Allergen-specific Immunoglobulin E (IgE) is integral to the pathogenesis of allergic disorders
- Binding of allergens to IgE antibodies on the surface of mast cells and basophils in sufficient quantities can lead to activation of the allergic response
- IgE-mediated allergic disorders include allergic asthma, allergic rhinitis, atopic dermatitis, and food allergies
- Omalizumab (Xolair) is the only approved anti-IgE therapy, indicated for allergic asthma with ongoing clinical development for peanut allergy
- Omalizumab has numerous limitations, including the need for repeated injections (every 2–4 weeks) and high cost
- **Unmet Need:** Novel therapies for the management of allergic disorders

Technology Overview

- **The Technology:** AAV gene therapy that provides sustained delivery of anti-IgE antibodies for the prevention of IgE-mediated allergic reactions
- The DNA sequence encoding for omalizumab was inserted into an AAV gene transfer vector (AAVrh.10anti-hIgE) and introduced into mice
- A humanized murine model of peanut allergy was generated by reconstituting immunodeficient mice with peanut-allergic human blood mononuclear cells
- **PoC Data:** A single dose of the gene therapy was sufficient for persistent prevention of peanut-induced sever allergy, both for prophylaxis and therapy after mice exhibit the peanut-induced anaphylaxis-related symptomology
- The inventors have also developed novel human anti-IgE antibodies with demonstrated efficacy that are ready to be incorporated into the AAV platform for further testing

Inventors:
Ronald Crystal
Odelya Pagovich
Maria Chiuchiolo

Patents:
US Patent 10,293,059
JP Patent JP6878301
CN Patent CN107635584B
CA Patent CA2982213C
EP Application Filed

Publications:
Pagovich et al. *J Allergy Clin Immunol*. 2016.

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Cornell Reference:
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Technology Applications

- One-time preventative therapy for peanut allergy and other severe, IgE-mediated allergic disorders
- Gene transfer method could be applied to other agents that block allergic reactions (e.g., soluble IgE receptors, eosinophils, and basophils)

Technology Advantages

- One-time therapy avoids the need for repeated and costly injections of omalizumab
- Durable protection improves patient quality of life by alleviating anxiety and risk associated with travel and dining at restaurants

Supporting Data / Figures

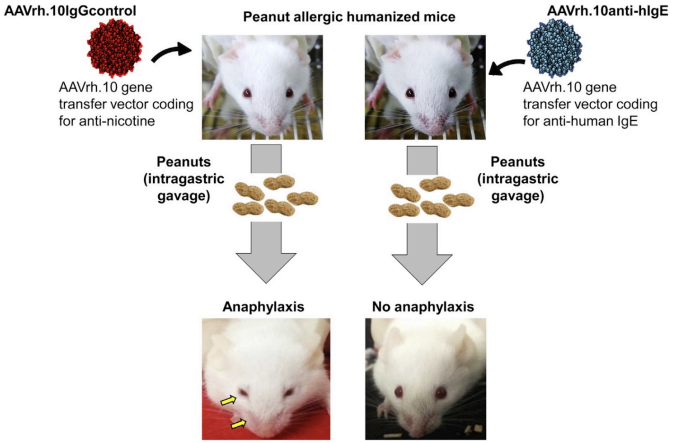

Figure 1: A single dose of an engineered AAV gene therapy coding for anti-human IgE provided significant protection against anaphylaxis in a humanized murine model of peanut allergy.

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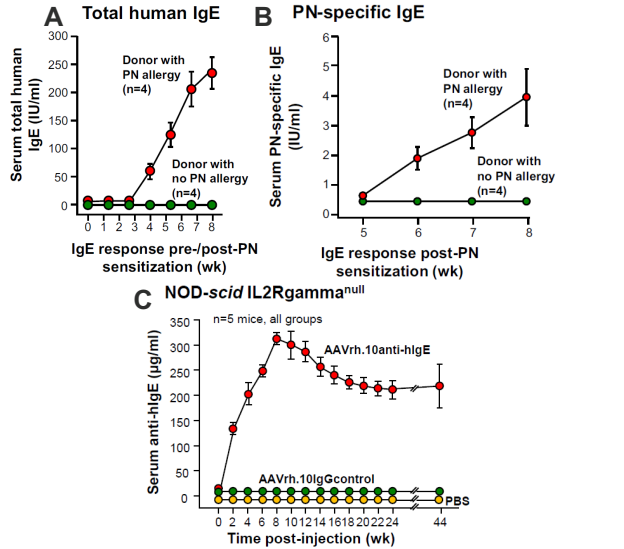

Figure 2: A-B: Reconstitution of immunodeficient mice with peanut (PN) allergic human blood mononuclear cells led to significant IgE induction. **C:** The anti-hIgE AAV gene therapy led to persistent induction of anti-hIgE (expression remained steady at 44 weeks).

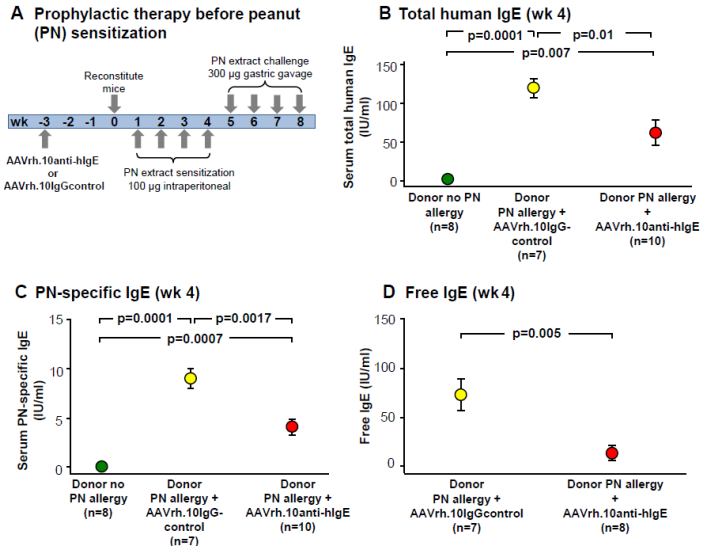

Figure 3: The anti-hIgE AAV gene therapy significantly reduced the IgE response to PN challenge in mice.

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