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LONGITUDINAL ANALYSIS OF SINGLE B CELLS, IGE ANTIBODIES, AND PLASMA IN A PEANUT ALLERGIC SUBJECT

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Introduction: Our understanding of monoclonal, allergen-specific IgE antibodies has been hindered by the scarcity of circulating IgE producing B cells, which are rare even in allergic individuals. The potential to isolate single B cells producing IgE antibodies and class switch these antibodies to IgG4 antibodies, like those that increase with allergen-specific immunotherapy, could be of great therapeutic value.

Methods: A 28-year-old peanut allergic subject donated 3 blood samples over a 4-month period in an IRB-approved study after qualifying with a peanut-specific IgE titer of >100 kUA/L. For each sample, IgE titers were measured by ImmunoCAP and monoclonal IgE antibody sequences from single B cells were identified using our single-cell RNA-sequencing discovery platform. We re-engineered these IgE antibodies as monoclonal IgG4 antibodies and characterized their binding specificity to peanut allergens such as Ara h 2.

Results: Peanut specific IgE and peanut allergen component IgE titers increased over the three visits, while total IgE fluctuated. In total, eight hundred IgE-producing B cells were isolated across the three visits. Next-generation sequencing analysis followed by antibody gene expression revealed the persistence of clonal families of related B cells that produced high affinity peanut-specific IgE antibodies. This occurred despite no clinical history of allergen exposure during this time.

Conclusion: The integration of single-cell transcriptomics, plasma diagnostic measurements, and antibody specificity yields novel insights into the persistence and evolution IgE antibodies. These results also highlight the potential for re-engineered antibodies to serve as therapeutics that may avoid long clinical response times and adverse events associated with food-based treatments.