Prediction of cumulative tolerated dose for peanut allergic children using epitope-specific IgE antibody profiling

Maria Suprun[1], Paul Kearney[2], Clive Hayward[2], Heather Butler[2], Robert Getts[2], Scott H. Sicherer[1], Paul J. Turner[3], Dianne E. Campbell[4], Hugh A. Sampson[1]

[1] Icahn School of Medicine at Mount Sinai; [2] AllerGenis LLC; [3] Imperial College London; [4] The University of Sydney

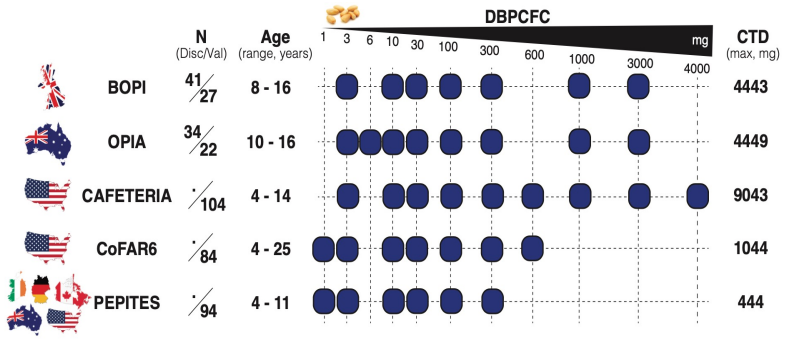
Introduction

- IgE-epitope profiling can accurately diagnose clinical peanut allergy [1].
- **Bead-Based Epitope Assay** {**BBEA**} utilizes bead-coupled peptides to measure IgE and IgG4 antibody levels. It is a highly reliable and sensitive assay for milk and peanut allergies [2].

Objective: To determine if sequential/linear epitope-specific IgE (**ses-IgE**) can provide probabilities of tolerating discrete doses of peanut protein in allergic subjects undergoing double-blind, placebo-controlled food challenges (DBPCFC) utilizing PRACTALL dosing.

Methods

Fig.1. *Study samples and DBPCFC dosing* (Disc – Discovery; Val – Validation).

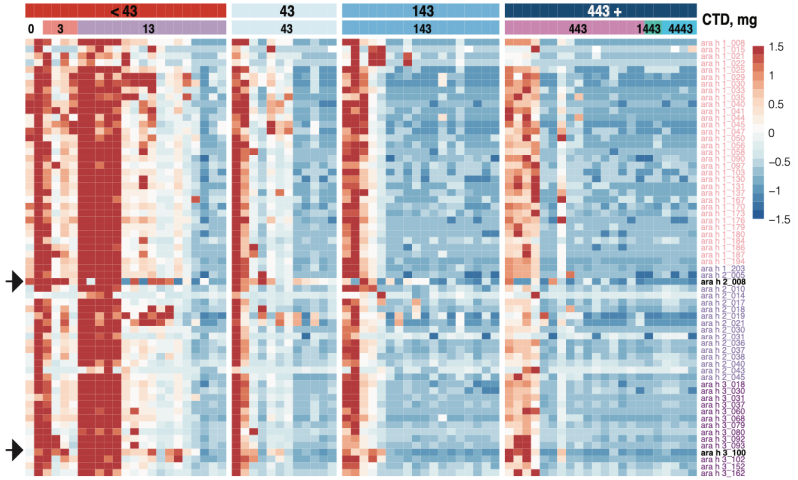


- 64 ses-IgE antibodies were measured by BBEA in plasma of subjects undergoing DBPCFC from five studies (Fig.1).
- 75 subjects from BOPI and OPIA were used in the Discovery phase, where
  - ➢ a pair of ses-IgEs that predicts Cumulative Tolerated Dose (**CTD**) was determined by machine learning (regressions) and evaluated using Spearman correlation (Rho).
  - ➢ ses-IgE predictor was validated on subjects from five independent cohorts.
- Validation subjects were grouped based on predicted values and probabilities of reactions at each CTD were calculated.

Ses-IgEs are associated with CTD

- In the Discovery cohort, patients reacting at lower CTDs generally having a greater number of epitopes recognized by IgEs (Fig.2).

Fig.2. *Patient-specific heatmap with all 64 ses-IgEs as rows*



- Correlations between CTD and individual ses-IgEs varied from -0.14 to -0.55, with >95% being statistically significant.

Ses-IgEs predictive of CTD

- Using machine learning in the Discovery phase, a pair of ses-IgEs that best predicts CTD was identified (Tab.1).

Tab.1. *Performance of top 3 models*

Ses-IgE #1	Ses-IgE #2	Rho p<0.05
Ara h 2_008	Ara h 3_100	0.61
Ara h 1_173	Ara h 3_100	0.59
Ara h 1_030	Ara h 3_100	0.58

- Significant correlation of a predicted score with actual CTD (Fig.3):
  - ➢ 0.61 in Discovery
  - ➢ 0.51 in Validation

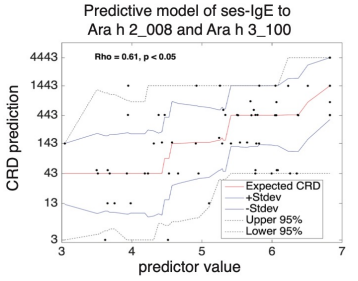
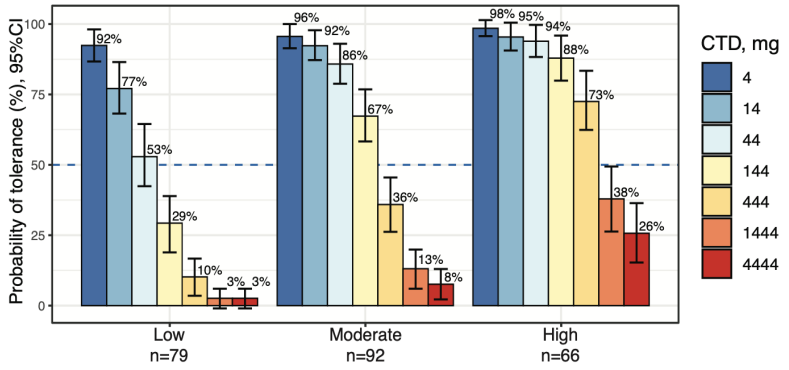


Fig.3. *Estimated CTD of a final model*

Predictor-based reaction probabilities

- Since the sample size at each dose tends to be small, further grouping was done based on ses-IgE predictor levels.
- Validation subjects were separated into three groups of dose reactivity: "low", "moderate", and "high" (Fig.4).

Fig.4. *Bar chart of probabilities of tolerance at each peanut dose by dose-reactivity groups in 237 Validation subjects*



- On average, subjects in the "high" dose-reactivity group were 4 times more likely to tolerate a specific dose, compared to the "low" dose group.

❖ Accurate predictions of thresholds are complex due to limited sample sizes at each dose and variations in study-specific DBPCFC protocols.

❖ This is a first validated algorithm using peanut specific epitopes to predict probabilities of reaction to different amounts of peanut in allergic subjects and may provide a useful surrogate for peanut food challenges.

References

1. Suárez-Fariñas M et al (2020). *Accurate and reproducible diagnosis of peanut allergy using epitope mapping.* Allergy

2. Suprun M et al (2019). *Novel Bead-Based epitope Assay is a sensitive and reliable tool for profiling epitope-specific antibody repertoire in food allergy.* Scientific Reports