The impact of filaggrin mutations in a large pediatric population with food allergy

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Aims: Loss-of-function-mutations in the epidermal barrier gene filaggrin (FLG) are the major genetic risk factor for eczema and eczema-associated allergic airways diseases. We aimed to investigate the role of FLG mutations in food allergy, the importance of which is still unclear.

Methods: We have recruited 523 children with food allergy diagnosed by double-blind placebo controlled food challenge. All children were extensively characterized including allergic responses to specific foods. The four most common FLG loss-of-function mutations were genotyped in all cases and controls. Association of FLG mutations with food allergy was analyzed by logistic regression using the Multicenter Allergy Study (MAS) as control population.

Results: FLG mutations were associated with allergies to diverse foods (hen’s egg, peanut, cow’s milk) with similar risk estimates (odds ratios between 2.5 and 2.7, P-values < 10^-5). Interestingly, this effect remained significant after adjusting for the eczema status. We did not observe an association of FLG mutations with polyvalent compared to monovalent food allergy. Mucocutaneous, gastrointestinal, respiratory, and cardiovascular responses during double-blind placebo controlled food challenge were documented in a standardized fashion. The FLG effect increased with the number of organ systems involved suggesting an effect on severity of the allergic response.

Discussion: Since FLG mutations cause a skin barrier defect, our results suggest a pathway for food allergy similar to that for eczema-associated asthma, where transcutaneous sensitization through the impaired epidermal barrier is the initializing event leading to localized or systemic allergic responses that may affect distant organ systems.

Conclusion: Co-occurrence of food allergy and eczema in early childhood is a common phenomenon. Using our large, well characterized food allergy cohort we demonstrated that FLG mutations confer risk for food allergy beyond their known association with eczema. They predispose to multi-organ involvement during allergic reactions, and should thus be considered when assessing anaphylaxis risk.