



Contents lists available at SciVerse ScienceDirect



Relating microarray component testing and reported food allergy and food-triggered atopic dermatitis: a real-world analysis

Irene Fung, MD^{*}; Jennifer S. Kim, MD[†]; and Jonathan M. Spergel, MD, PhD^{*}

^{*} Division of Allergy and Immunology, Children's Hospital of Philadelphia, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

[†] Division of Allergy and Immunology, Department of Pediatrics, Jaffe Food Allergy Institute, Mount Sinai School of Medicine, New York, New York

ARTICLE INFO

Article history:

Received for publication September 4, 2012.

Received in revised form November 6, 2012.

Accepted for publication December 9, 2012.

ABSTRACT

Background: High epitope diversity has been associated with increased IgE-mediated food allergy severity.

Objective: To characterize associations between results from an automated microarray system and self-reported food allergy and food-triggered atopic dermatitis (AD).

Methods: Families with food allergic children were identified from a Jewish community in Lakewood, New Jersey, with immediate family members without food allergy or food-triggered AD serving as controls for the identified children. Sets of microarray components analyzed were to milk (Bos d 4, Bos d 5, Bos d 8, Bos d lactoferrin), egg (Gal d 1, Gal d 2, Gal d 3, Gal d 5), and peanut (Ara h 1, Ara h 2, Ara h 3, Ara h 6).

Results: Seventy-three patients from 23 families were recruited. Culprit foods included milk (n = 20), egg (n = 10), and peanut (n = 6) for food allergy and milk (n = 10) and egg (n = 7) for food-triggered AD. Odds of having had a self-reported related food allergy or food-triggered AD reaction significantly increased with a higher number of detectable microarray components to that food. Ara h 1, Ara h 2, and Ara h 6 were individually associated with reported peanut allergy, and Bos d 4 was individually associated with reported milk allergy. The number of egg components significantly increased the odds of having related food-triggered AD.

Conclusion: High diversity of food allergen components relates well to self-reported history of food allergy and food-associated AD.

© 2012 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Introduction

Food allergy is a common disease that affects 2% to 10% of the population.^{1–4} The criterion standard for diagnosis is a double-blind, placebo-controlled food challenge. However, this challenge is not always performed because of resource unavailability and potential reaction risk. More commonly, a food allergy diagnosis is made based on clinical history combined with skin prick test (SPT) and/or fluorescence enzyme immunoassay (FEIA). These investigations have their limitations. Although both SPT and FEIA have a high sensitivity of greater than 85%, specificity is lower at 40% to 80%.⁵ FEIA can yield a 95% positive predictive value in some foods⁶; however, because whole food extracts are used in FEIA, results may be falsely positive if the patient generates IgE antibodies against cross-reactive allergens or epitopes within the food that are not clinically relevant to inducing an allergic reaction. In patients with atopic dermatitis (AD), test result interpretation can be particularly difficult. No clinical decision points have been identified for eczematous reactions.⁷ Although eczematous reactions can be seen

on food challenge in children with AD, in one study the FEIA sensitivity and specificity were low at 68% and 50%, respectively.⁸

Component-resolved diagnosis by microarray is a novel method of analyzing food allergy. A specific panel of purified or recombinant protein components for each food extract is provided within a microarray, and detection for host-specific IgE antibody to these proteins is identified. Microarray assessment permits quantitative data to be collected in a robust fashion, which may help better characterize food allergy. In addition, automated microarray systems that are now commercially available are potentially cheaper and may be more efficient and more accurate than serologic whole allergen specific IgE techniques.⁵ Epitope diversity has been demonstrated in prior studies to correlate with reaction severity of patients with food allergies to peanut,^{4,9,10} milk,^{3,11–13} and egg.^{2,14} Thus, we wondered whether identification of the component diversity of an automated microarray system (ISAC; Thermo Fisher Scientific, Waltham, Massachusetts) could be used to clinically diagnose food allergy. In addition, prior studies of microarray-based IgE detection have included individuals with food-exacerbated AD within their food allergic cohort,^{15,16} which could cloud results given additional non-IgE-mediated mechanisms in AD.^{17,18} Thus, we separated this subset in our analysis. The purpose of our study was to assess the utility of a newly available automated system using microarray technology reporting in

Reprints: Jonathan M. Spergel MD, PhD, Division of Allergy and Immunology, 3550 Market St, Philadelphia, PA 19104; E-mail: spergel@email.chop.edu.

Disclosures: Authors have nothing to disclose.

Funding Sources: Funding for this study was provided by grant A-16809.2 and grant W81XWH-11-1-0507 (to Dr Spergel) from the US Department of Defense.

a semiquantitative determination of units (ISAC). We wanted to see how this corresponded to patient-reported food allergy and food-triggered AD. First, we analyzed odds ratios (ORs) using self-reported food allergy reactions to milk, egg, and peanut as independent variables. Dependent variables included the diversity of detectable components and specific individual detectable components. Second, we looked at how well these variables related to reported milk-, egg-, and peanut-related AD, using the same method.

Methods

Participants in this study were part of a cohort for an ongoing food allergy genetics study for which data have not yet been published. Recruitment occurred during a food allergy informational session presented at a community town hall meeting in Lakewood, New Jersey. This community is composed of 54,500 members of Jewish descent,¹⁹ for which a driving force for migration into this area was the establishment of the Lakewood Yeshiva in 1943.²⁰ A sign-up sheet was provided for families who reside in the area interested in participating in food allergy research. To be included, participants had to be either a child with reported food allergy and/or food-associated AD or an immediate family member (biological parent or sibling) of this child. Approval was obtained from the Children's Hospital of Philadelphia institutional research board and written informed consent obtained from all research participants. A senior investigator (J.M.S.) concluded that history of food allergy along with skin test and specific IgE when available were consistent with IgE-mediated food allergy. We used established criteria adapted from Thompson and Hanifen²¹ (eTable 1). Return visits to Lakewood were scheduled for blood collection for microarray tests (eg, ImmunoCAP and ISAC). Components assessed on the ISAC chip were to milk (Bos d 4, Bos d 5, Bos d 8, Bos d lactoferrin), egg (Gal d 1, Gal d 2, Gal d 3, Gal d 5), and peanut (Ara h 1, Ara h 2, Ara h 3, Ara h 6). Components were considered positive if the result was 0.3 ISAC standardized units (ISU) or more.²² Summary statistics were performed using STATA12 statistical software (StataCorp, College Station, Texas). $P < .05$ was considered significant. Logistic regression was used to determine whether positivity for individual microarray components or diversity of components significantly increased the odds of having corresponding self-reported food allergy or food-associated AD. For individual components, we calculated sensitivity, specificity, positive predictive value, and negative predictive value. Because there were multiple peanut components of significance, we developed a scoring tool to relate the number of positive peanut components to reported IgE-mediated food allergy. We adapted a previously used scoring system²³ and assigned a score of +3 to highly significant variables ($P < .001$), a score of +2 to those with P values between $<.001$ and $.005$, and score of +1 to those with P values between $.005$ and $.05$. We then reviewed how well these scores related to reported food symptoms.

Results

Seventy-three patients from 23 families were recruited. Demographic information regarding age, sex, atopy, and adverse reactions to food are listed in Table 1. Of the 20 patients with self-reported milk food allergy, 13 had SPT and/or FEIA above a 95% predictive decision point,^{6,24} 3 had positive testing not above this threshold, and 4 had no available records. For the 10 patients with self-reported egg allergy, 7 had SPT and/or FEIA at above the 95% predictive decision point, 2 had positive test results not above this threshold, and 1 did not have available test results. Among the 6 individuals with self-reported peanut allergy, 3 had SPT or FEIA above the 95% positive predictive value threshold, 1 had a positive test result not above this threshold, and 2 did not have available

Table 1

Demographic characteristics of the study patients^a

Characteristic	No. (%) of patients (N = 73)
Age, mean (range), y	10 (1–38)
Male	39 (53)
Asthma	16 (22)
Allergic rhinitis	21 (29)
Food allergy	23 (32)
Atopic dermatitis	21 (29)
Specific food allergies	
Milk	20 (27)
Egg	10 (14)
Peanut	6 (8)
Other foods	19 (26)
Food-related atopic dermatitis	
Milk	10 (14)
Egg	7 (10)
Peanut	2 (3)
Other foods	3 (4)

^aData are presented as number (percentage) of patients unless otherwise indicated.

records. Other foods perceived to have caused IgE-mediated symptoms on ingestion were sesame ($n = 10$), tree nuts ($n = 7$), fish ($n = 2$), and soy ($n = 1$). For reported food-triggered AD, milk, egg, peanut, wheat, and sesame were reported triggers.

Relating ISAC Component Diversity to Self-reported Food Allergy

The odds were significantly higher in patients with greater component diversity for the culprit foods, as indicated in Table 2 (peanut: OR, 10.2; 95% confidence interval [CI], 2.08–49.75; $P < .004$; milk: OR, 38.7; 95% CI, 6.05–247.24; $P < .001$; egg: OR, 3.34; 95% CI, 1.50–7.43; $P < .003$). The odds of reported IgE-mediated peanut allergy were also significant for individually positive Ara h 1, Ara h 2, and Ara h 6, whereas for milk, Bos d 4 was significant.

We then assessed Ara h 1, Ara h 2, and Ara h 6 within the context of the aforementioned scoring tool. The points allotted for each component were based on the P values (Table 1). No component reached $P < .001$. With this tool, 50 of 53 patients who tolerated peanut were correctly identified with a score of zero. The remaining 3 patients each had a score of 3. All 6 patients with reported IgE-mediated reactions to peanut had positive scores. Five of these patients had a score of 4 and 1 had a score of 2.

Table 2

Logistic regression analysis evaluating the association between microarray component outcomes and history of reported IgE-mediated food allergy reaction

Food	OR (95% CI)	P value	Score
Peanut			
Ara h 1	1.15 (1.03–1.28)	.02	+1
Ara h 2	1.29 (1.08–1.52)	.003	+2
Ara h 3	...		
Ara h 6	1.16 (1.03–1.31)	.01	+1
No. of positive components	10.16 (2.08–49.75)	.004	
Milk			
Bos d 4	9.21 (1.96–43.4)	.005	
Bos d 5	...		
Bos d 8	...		
Bos d lactoferrin	1.41 (0.25–7.80)	.69	
No. of positive components	38.67 (6.05–247.24)	<.001	
Egg			
Gal d 1	1.17 (0.96–1.41)	.11	
Gal d 2	1.60 (0.86–2.96)	.14	
Gal d 3	1.03 (0.71–1.48)	.89	
Gal d 5	...		
No. of positive components	3.34 (1.50–7.43)	.003	

Abbreviations: CI, confidence interval; OR, odds ratio.

^aEllipses indicate inadequate sample size available to perform logistic regression.

Table 3

Sensitivities and Specificities of Microarray Components in Predicting Reported IgE-Mediated Food Allergy

Food	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Peanut				
Ara h 1	100	98	86	100
Ara h 2	83	96	71	98
Ara h 3	33	100	71	98
Ara h 6	83	96	71	88
Milk				
Bos d 4	65	98	93	88
Bos d 5	60	100	100	87
Bos d 8	45	100	100	83
Bos d lactoferrin	5	98	50	73
Egg				
Gal d 1	40	96	67	90
Gal d 2	20	98	67	90
Gal d 3	30	94	50	8
Gal d 5	20	100	100	87

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

In general, individual components had high specificities but lower sensitivities (Table 3). For peanut, sensitivity and specificity was highest for Ara h 1, at 100% and 98%, respectively. Specificities of individual milk and egg were similarly high (range, 96%–100%). A logistic regression analysis looking at FEIA values for these foods and reported food allergy was not significant in any of these foods (data not shown).

Relating Microarray Component Diversity to Reported Food-Triggered AD

Culprit foods implicated in food-triggered AD included milk ($n = 10$), egg ($n = 7$), and peanut ($n = 2$). Peanut-triggered AD was not analyzed because of low numbers of cases. Results are listed in Table 4. For egg-triggered AD, the number of positive components reached statistical significance as a dependent variable (OR, 2.21; 95% CI, 1.07–4.56; $P = .03$). Individual components did not reach significance. Table 5 lists the calculated sensitivity and specificity of individual components for milk- and egg-associated AD. In general, individual components and combined numbers of components had high specificity for milk (range, 75%–97%) and egg (range, 91%–98%) but had relatively lower sensitivities (0%–38% for milk and 0%–38% for egg).

Discussion

Our results suggest that a high number of food components are a good indicator of food IgE-mediated allergy. Of interest to us, prior

Table 4

Logistic Regression Analysis Evaluating the Association Between Milk and Egg Microarray Component Outcomes and History of Reported Food-Triggered Atopic Dermatitis

Food	OR (95% CI)	P value
Milk		
Bos d 4	1.04 (0.89–1.22)	.63
Bos d 5	1.02 (0.88–1.17)	.83
Bos d 8	1.06 (0.79–1.42)	.71
Bos d lactoferrin	...	
No. of positive components	1.63 (0.92–2.87)	.09
Egg		
Gal d 1	2.05 (0.56–7.51)	.28
Gal d 2	3.81 (0.45–32.65)	.22
Gal d 3	1.95 (0.82–4.62)	.13
Gal d 5	...	
No. of positive components	2.21 (1.07–4.56)	.03

Abbreviations: CI, confidence interval; OR, odds ratio.

aEllipses indicate inadequate sample size available to perform logistic regression.

Table 5

Sensitivities and Specificities of Milk and Egg Microarray Components in Predicting Reported Food-Triggered Atopic Dermatitis

Food	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Milk				
Bos d 4	38	82	20	91
Bos d 5	38	86	25	92
Bos d 8	34	86	27	86
Bos d lactoferrin	0	97	0	89
Egg				
Gal d 1	38	95	50	91
Gal d 2	33	98	67	93
Gal d 3	25	93	67	90
Gal d 5	0	96	0	87

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

studies have identified certain components to be more specific than others for discriminating allergy; however, these components appear to have difference prevalence rates, depending on the population studied. For example, Ara h 1 was detected in more than 90% of peanut-sensitive American patients by Burks et al,²⁵ whereas Beyer²⁶ reported 75% prevalence. Clarke et al²⁷ found 73% prevalence in United Kingdom subjects, and Kleber-Janke et al²⁸ found 65% prevalence in a German cohort. Vereda et al²⁹ found immunologic differences among Spanish, Swedish, and US populations, with Ara h 2 being lowest in the Spanish group. Our Lakewood community was a unique, geographically homogeneous cohort in which Ara h 1, Ara h 2, and Ara h 6 were all significantly related to reported food allergy. Our pilot scoring tool incorporating these peanut components was helpful in relating to reported food allergy. In the future, a validated scoring tool incorporating significant components to predict food allergy could significantly affect management. Future studies using oral food challenge as the standard for comparison are therefore very much desired.

In our analysis of egg components, Gal d 1 had high specificity (96%) for reported food allergy. Its sensitivity (40%) was higher than other egg components. These results are consistent with other studies, which suggest that Gal d 1 is the immunodominant epitope in persistent egg allergy.^{14,30–32} In regard to milk components, Bos d 8 did not have a higher specificity and sensitivity compared with other components. This finding is in contrast to finding from D'Urbano et al¹⁷ that the most commonly detected milk component in children with positive milk oral challenge results was Bos d 8 (46.5%). Because this study was performed in Italy, geographic variation is one variable that may account for this difference.

Few studies to date address the role of microarray testing in diagnosing food-triggered AD. In 20 adult patients with AD, 65% had detectable cross-allergens, such as birch Bet v 1, alder Aln g 1, apple Mal d 1, and celery Api g 1.³³ In pediatric studies, results from patients with food-triggered AD were combined with those from patients with type 1 mediated food allergy. Egger et al¹⁶ reported that Gal d 1 and Gal d 2 were the major detectable components in 25 children with suspected egg allergy, 16 of which had flare of their AD on oral food challenge. Within a cohort of egg and/or milk allergic patients studied for developing microarray clinical decision points for oral food challenge prediction, 8% demonstrated AD exacerbation on double-blinded, placebo-controlled oral food challenge. More recently, Hochwallner et al³⁴ found that patients who reported skin-only symptoms to milk had lower numbers and amounts of detectable components on microarray compared with those with reported severe systemic reactions. In our study, we found that the number of positive egg components significantly increased the odds of having had reported egg-triggered AD. Further validation of this association and similar relationships for other foods requires larger sample sizes and double-blinded, placebo-controlled food allergy testing.

The ISAC has several potential benefits. It requires a small amount of blood, and many different allergens can be assessed at once, particularly for those with multiple food allergies. Performance-wise, 2 studies reported that microarray testing was comparable to FEIA in predicting milk- and egg-positive oral food challenge results.^{15,17} We demonstrated that ISAC microarray results relate well to reported food reactions. Thus, currently ISAC microarray testing may be a helpful adjunct test to SPT and FEIA, which have high sensitivities but low specificities. In the future, with increased diagnostic accuracy of microarray, as reported by Lin et al.⁹ using bioinformatics methods, we anticipate that microarray testing will become a more valuable adjunctive method of investigating food allergy.

The first limitation to our study is that oral food challenges were not performed to substantiate food allergy histories. Although we could not verify the reported food-related reactions, we identified food allergy cases based on histories with timing and symptoms consistent with such a reaction.^{35,36} Second, many patients with reported milk, egg, or peanut food allergy had prior documentation of positive SPT and/or IgE test results to the culprit food. Within the group, 9 patients had records of milk FEIA, 12 had egg FEIA, and 12 had peanut FEIA. Nonetheless, for food-related AD, parent history can lack sensitivity,⁸ and thus oral challenges are needed to support our findings for this group. A third limitation is that we studied a population in one geographic setting; thus, results may not be generalizable to other groups. This limitation may explain why Ara h 2 did not have higher specificity compared with other peanut components, as has been found previously in a pediatric population from the United Kingdom.^{37,38} Nonetheless, our findings are in keeping with prior studies and suggest that the ISAC immunoassay is a useful additional tool for food allergy diagnosis.^{37,39} Future studies should be performed to validate efficacy of the microarray immunoassay in clinical practice.

In conclusion, we report that high diversity of detectable peanut, egg, and milk allergen components relates well to reported allergy reaction to these suspected foods, as does increased total sum of peanut and milk components but to a lesser degree. With proper development of a scoring tool, this serologic testing may become valuable in predicting food allergy.

Acknowledgments

We thank Kathryn Ruymann, Megan Ott, and Rosetta Chiavacchi for their help with data collection.

Supplementary Data

Supplementary data related to this article can be found at doi:10.1016/j.anai.2012.12.006

References

- [1] Chafen JJ, Newberry SJ, Riedl MA, et al. Diagnosing and managing common food allergies: a systematic review. *JAMA*. 2010;303:1848–1856.
- [2] Cooke SK, Sampson HA. Allergenic properties of ovomucoid in man. *J Immunol*. 1997;159:2026–2032.
- [3] Chatchatee P, Jarvinen KM, Bardina L, Beyer K, Sampson HA. Identification of IgE- and IgG-binding epitopes on alpha(s1)-casein: differences in patients with persistent and transient cow's milk allergy. *J Allergy Clin Immunol*. 2001;107:379–383.
- [4] Shreffler WG, Beyer K, Chu TH, Burks AW, Sampson HA. Microarray immunoassay: association of clinical history, in vitro IgE function, and heterogeneity of allergenic peanut epitopes. *J Allergy Clin Immunol*. 2004;113:776–782.
- [5] Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol*. 2008;100(3 suppl 3):S1–S148.
- [6] Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol*. 2001;107:891–896.
- [7] Werfel T, Ballmer-Weber B, Eigenmann PA, et al. Eczematous reactions to food in atopic eczema: position paper of the EAACI and GA2LEN. *Allergy*. 2007;62:723–728.
- [8] Breuer K, Heratizadeh A, Wulf A, et al. Late eczematous reactions to food in children with atopic dermatitis. *Clin Exp Allergy*. 2004;34:817–824.
- [9] Lin J, Bruni FM, Fu Z, et al. A bioinformatics approach to identify patients with symptomatic peanut allergy using peptide microarray immunoassay. *J Allergy Clin Immunol*. 2012;129:1321–1328.
- [10] Flinterman AE, Knol EF, Lencer DA, et al. Peanut epitopes for IgE and IgG4 in peanut-sensitized children in relation to severity of peanut allergy. *J Allergy Clin Immunol*. 2008;121:737–743.
- [11] Chatchatee P, Jarvinen KM, Bardina L, Vila L, Beyer K, Sampson HA. Identification of IgE and IgG binding epitopes on beta- and kappa-casein in cow's milk allergic patients. *Clin Exp Allergy*. 2001;31:1256–1262.
- [12] Wang J, Lin J, Bardina L, et al. Correlation of IgE/IgG4 milk epitopes and affinity of milk-specific IgE antibodies with different phenotypes of clinical milk allergy. *J Allergy Clin Immunol*. 2010;125:695–702.
- [13] Jarvinen KM, Chatchatee P, Bardina L, Beyer K, Sampson HA. IgE and IgG binding epitopes on alpha-lactalbumin and beta-lactoglobulin in cow's milk allergy. *Int Arch Allergy Immunol*. 2001;126:111–118.
- [14] Jarvinen KM, Beyer K, Vila L, Bardina L, Mishoe M, Sampson HA. Specificity of IgE antibodies to sequential epitopes of hen's egg ovomucoid as a marker for persistence of egg allergy. *Allergy*. 2007;62:758–765.
- [15] Ott H, Baron JM, Heise R, et al. Clinical usefulness of microarray-based IgE detection in children with suspected food allergy. *Allergy*. 2008;63:1521–1528.
- [16] Egger M, Alessandri C, Wallner M, et al. Is aboriginal food less allergenic? comparing IgE-reactivity of eggs from modern and ancient chicken breeds in a cohort of allergic children. *PLoS One*. 2011;6:e19062.
- [17] D'Urbano LE, Pellegrino K, Artesani MC, et al. Performance of a component-based allergen-microarray in the diagnosis of cow's milk and hen's egg allergy. *Clin Exp Allergy*. 2010;40:1561–1570.
- [18] Oyoshi MK, He R, Kumar L, Yoon J, Geha RS. Cellular and molecular mechanisms in atopic dermatitis. *Adv Immunol*. 2009;102:135–226.
- [19] Sheskin L. *Jewish Population in the United States, 2011*. Current Jewish Population Reports. Storrs: Berman Institute, North American Jewish Data Bank, University of Connecticut; 2012.
- [20] Fahim K. *As Orthodox Population Grows, So Do Tensions*. New York Times; December 10, 2007.
- [21] Thompson MM, Hanifin JM. Effective therapy of childhood atopic dermatitis allays food allergy concerns. *J Am Acad Dermatol*. 2005;53(2 suppl 2):S214–S219.
- [22] Directions for use ImmunoCAP ISAC Kit IgE. <http://www.phadia.com/Global/Corporate%20Allergy/Files/DFU/Assay%20Kit%20IgE/DFU-ImmunoCAP-ISAC-20-01-02-3-RUO.pdf>. Accessed January 5, 2009.
- [23] Maric I, Robyn J, Metcalfe DD, et al. KIT D816V-associated systemic mastocytosis with eosinophilia and FIP1L1/PDGFR α -associated chronic eosinophilic leukemia are distinct entities. *J Allergy Clin Immunol*. 2007;120:680–687.
- [24] Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin Exp Allergy*. 2000;30:1540–1546.
- [25] Burks AW, Williams LW, Helm RM, Connaughton C, Cockrell G, O'Brien T. Identification of a major peanut allergen, Ara h 1, in patients with atopic dermatitis and positive peanut challenges. *J Allergy Clin Immunol*. 1991;88:172–179.
- [26] Beyer K. Characterization of allergenic food proteins for improved diagnostic methods. *Curr Opin Allergy Clin Immunol*. 2003;3:189–197.
- [27] Clarke MC, Kilburn SA, Hourihane JO, Dean KR, Warner JO, Dean TP. Serological characteristics of peanut allergy. *Clin Exp Allergy*. 1998;28:1251–1257.
- [28] Kleber-Janke T, Cramer R, Appenzeller U, Schlaak M, Becker WM. Selective cloning of peanut allergens, including profilin and 2S albumins, by phage display technology. *Int Arch Allergy Immunol*. 1999;119:265–274.
- [29] Vereda A, van HM, Ahlstedt S, et al. Peanut allergy: clinical and immunologic differences among patients from 3 different geographic regions. *J Allergy Clin Immunol*. 2011;127:603–607.
- [30] Alessandri C, Zennaro D, Scala E, et al. Ovomucoid (Gal d 1) specific IgE detected by microarray system predict tolerability to boiled hen's egg and an increased risk to progress to multiple environmental allergen sensitisation. *Clin Exp Allergy*. 2012;42:441–450.
- [31] Urisu A, Yamada K, Tokuda R, et al. Clinical significance of IgE-binding activity to enzymatic digests of ovomucoid in the diagnosis and the prediction of the outgrowing of egg white hypersensitivity. *Int Arch Allergy Immunol*. 1999;120:192–198.
- [32] Urisu A, Ando H, Morita Y, et al. Allergenic activity of heated and ovomucoid-depleted egg white. *J Allergy Clin Immunol*. 1997;100:171–176.
- [33] Ott H, Folster-Holst R, Merk HF, Baron JM. Allergen microarrays: a novel tool for high-resolution IgE profiling in adults with atopic dermatitis. *Eur J Dermatol*. 2010;20:54–61.
- [34] Hochwallner H, Schulmeister U, Swoboda I, et al. Microarray and allergenic activity assessment of milk allergens. *Clin Exp Allergy*. 2010;40:1809–1818.

- [35] Food allergy: a practice parameter. *Ann Allergy Asthma Immunol*. 2006; 96(3 suppl 2):S1–S68.
- [36] Adverse Reactions to Foods. In: Adkinson N, Busse W, Bochner BS, Holgate S, Simons E, Lemanske Jr RF, eds. *Middleton's Allergy: Principles and Practice*. Philadelphia, PA: Elsevier; 2008.
- [37] Nicolaou N, Poorafshar M, Murray C, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol*. 2010;125:191–197.
- [38] Nicolaou N, Murray C, Belgrave D, Poorafshar M, Simpson A, Custovic A. Quantification of specific IgE to whole peanut extract and peanut components in prediction of peanut allergy. *J Allergy Clin Immunol*. 2011;127: 684–685.
- [39] Beyer K, Ellman-Grunther L, Jarvinen KM, Wood RA, Hourihane J, Sampson HA. Measurement of peptide-specific IgE as an additional tool in identifying patients with clinical reactivity to peanuts. *J Allergy Clin Immunol*. 2003;112:202–207.

eTable 1

Food Allergy and Food-Associated Atopic Dermatitis Questionnaire

1. Do you feel that food contributes to your child's eczema?
2. Has your child ever had an allergic reaction to a food or foods?
 1. If so, which food(s)?
 2. What reaction occurred?
 1. Hives
 2. Lip/face swelling
 3. Swelling/tightening of mouth/throat
 4. Chest tightening, wheezing or cough
 5. Vomiting, diarrhea or cramping
 6. Worsening of eczema (describe)
 7. Other symptoms (describe)
 3. How quickly after eating did the reaction occur?
 4. Has your child had any type of testing for allergy? If so, what test?