

LETTER TO THE EDITOR

Apparent IgE negative anaphylactic reaction to banana combined with kiwi allergy – complementary diagnostic value of purified single banana allergens

Editor

Allergists in practise are confronted with the deplorable fact that more and more standardized routine diagnostic solutions are no longer available for skin prick test (SPT) since pharmaceutical industries do not apply for the extension of the respective marketing authorization due to complex reasons. This leaves allergists with natural allergen sources as test agents and all disadvantages of non-standardized prick-material, particularly severe side-effects and false-positive reactions.

We report a case of banana anaphylaxis combined with kiwi allergy in which IgE concentrations, as detected with routine diagnostic measures, did not at all mirror the sensitization causing the symptoms. A 29-year-old non-atopic woman experienced rhinitis, facial oedema and dyspnoea 10–15 min after consumption of green kiwi fruit. Two weeks later, she developed rhinitis, oedema of the eye lids and laryngeal oedema after ingestion of half a banana. SPT to commercially available common food and inhalant allergens were negative. Prick-to-prick test with the suspected allergen sources (raw fruits) was positive; kiwi fruit: 8 mm; banana: 5 mm. *In vitro* routine allergy diag-

nostic tests *via* CAP-FEIA revealed no IgE reactivity to banana extract. In contrast, specific IgE to green kiwi extract was 0.679 kU/l (Table 1).

For kiwi fruit (*Actinidia deliciosa*, Act d) allergy diagnosis, 4/11 identified¹ and WHO/IUIS-documented allergens are available for routine IgE detection in ISAC microarray (ThermoFisher Scientific, Freiburg, Germany): Act d 1 (actinidin, a cysteine protease); Act d 2 (thaumatin-like protein, TLP); Act d 5 (kiwel-lin) and Act d 8 (Bet v 1-homologue). IgE detection *via* ISAC revealed a positive IgE reaction against Act d 2 (1.0 ISU-E) and IgE negativity to Act d 1, 5 and 8 (Table 1). However, in contrast to these results, a subsequently performed immunoblot with kiwi extract, purified Act d 1 and Act d 2 revealed an IgE reaction of the serum not only to Act d 2 (thereby confirming ISAC), but to Act d 1 as well (Fig. 1a).^{2,3}

Routine allergen-specific IgE antibody detection based upon aqueous extracts is often not sufficient to detect IgE against single allergens which are underrepresented in the whole extract, for which banana is only one example. To address this issue, three single banana allergens (Mus a 2, chitinase; Mus a 4, TLP and Mus a 5, β -1,3-glucanase) were purified and used as targets in immunoblot.^{4–6} None of these allergens is available for routine allergy diagnostic tests so far. In the immunoblot, the serum-IgE reacted with several proteins in the banana extract and all three single allergens (Mus a 2, 4, and 5; Fig. 1b), which are obviously underrepresented in the *in vitro* routine diagnostic extracts.

Act d 2 (like Mus a 4) is a TLP, a group of food allergens of which the allergenic potential is still not entirely clear. However,

Table 1 Synopsis of IgE detection results for whole allergen extracts *via* CAP-FEIA (ImmunoCAP) and component-resolved diagnosis as obtained *via* CAP-FEIA (ImmunoCAP) and ISAC

	Target Whole allergen extract	CAP-FEIA IgE [kU/l]	Target Single allergen	CAP-FEIA IgE [kU/l]	ISAC IgE [ISU-E]
Birch pollen (<i>Betula verrucosa</i>)	Birch pollen	Neg.	rBet v 1	Neg.	Neg.
			rBet v 2	Neg.	Neg.
Banana (<i>Musa acuminata</i>)	Banana	Neg.		NA	NA
Kiwi fruit (<i>Actinidia deliciosa</i>)	Kiwi	0.679	rAct d 1	NA	Neg.
			rAct d 2	NA	1.0*
			rAct d 5	NA	Neg.
			rAct d 8	Neg.	Neg.
Natural rubber latex	Whole extract	Neg.	Hev b 1,3,5,6,8	ND	Neg.
Bromelain	ND	ND	MUXF	ND	Neg.

Neg., negative; ND, not determined; NA, not available.

*Clinically relevant; serum tryptase: 2.9 μ g/L; total serum IgE: 16.3 kU/L.

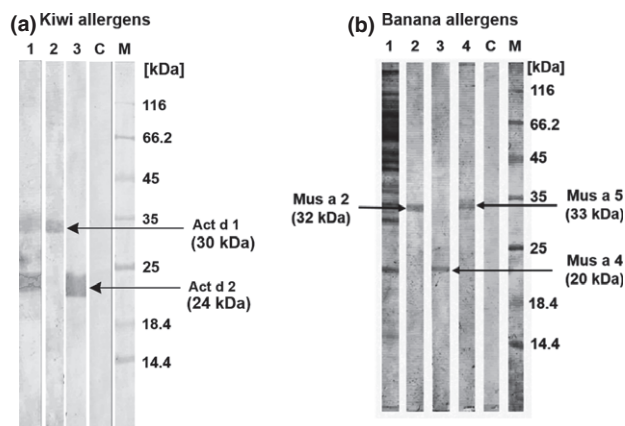


Figure 1 (a) Analysis of kiwi fruit allergens with serum from patient 431. Lane 1. kiwi fruit extract; 2. Act d 1; 3. Act d 2; C. secondary and tertiary antibody control; M. molecular weight markers. (b) Analysis of banana allergens with serum from patient 431. Lane 1. banana fruit extract; 2. Mus a 2; 3. Mus a 4; 4. Mus a 5; C. Secondary and tertiary antibody control; M. molecular weight markers.

as shown in this study, TLPs may not only be of clinical significance, they may also be the reason why the patient reacted to kiwi and cross-reacted to banana 2 weeks later. A sequence alignment revealed an identity of 69% between the TLPs of banana (Mus a 4) and kiwi (Act d 2) on amino acid level⁷ so that a connection between these two food allergies via cross-reactivity is highly probable.

This case shows that relevant allergenic banana proteins are underrepresented in routine diagnostic extracts with the consequence of false-negative IgE results and most probably an unknown prevalence of banana allergy. As exemplified by our report, additional use of component-resolved allergy diagnostics increases sensitivity and specificity of routine extract-based allergy diagnostic measures. Since well-standardized skin test solutions of clinically relevant allergen sources are expected to be sincerely reduced in near future, it is most important to consolidate valid diagnostic alternatives.

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References

- 1 Le TM, Bublin M, Breiteneder H *et al*. Kiwifruit allergy across Europe: clinical manifestation and IgE recognition patterns to kiwifruit allergens. *J Allergy Clin Immunol* 2013; **131**: 164–171.
- 2 Gavrovic-Jankulovic M, Cirkovic T, Vuckovic O *et al*. Isolation and biochemical characterization of a thaumatin-like kiwi allergen. *J Allergy Clin Immunol* 2002; **110**: 805–810.
- 3 Grozdanovic M, Popovic M, Polovic N *et al*. Evaluation of IgE reactivity of active and thermally inactivated actinidin, a biomarker of kiwifruit allergy. *Food Chem Toxicol* 2012; **50**: 1013–1018.
- 4 Palacin A, Quirce S, Sanchez-Monge R *et al*. Sensitization profiles to purified plant food allergens among pediatric patients with allergy to banana. *Pediatr Allergy Immunol* 2011; **22**: 186–195.
- 5 Aleksic I, Popovic M, Dimitrijevic R *et al*. Molecular and immunological characterization of Mus a 5 allergen from banana fruit. *Mol Nutr Food Res* 2012; **56**: 446–453.
- 6 Nikolic J, Mrkic I, Grozdanovic M *et al*. Isolation protocol for three important banana allergens. *J Chromatogr B Analyt Technol Biomed Life Sci* 2014; **962C**: 30–36.
- 7 Clendennen SK, May GD. Differential gene expression in ripening banana fruit. *Plant Physiol* 1997; **115**: 463–469.

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