## IDENTIFICATION OF POTENTIAL ALLERGENS INVOLVED IN SYSTEMIC REACTIONS TO MELON AND WATERMELON

Muskmelon (*Cucumis melo*) is a fruit that belongs to the Cucurbitaceae family. Muskmelon (hereafter *melon*) allergy is highly prevalent in several geographic areas (Central and Mediterranean Europe and the United States).[1,2] Melon is 1 of the fruits more frequently involved in allergic symptoms in Spain. Oral allergy syndrome is usually its main manifestation, and systemic reactions are rare in patients with melon or watermelon allery.[1,2] Three allergens have been identified in melon: cucumisin (Cuc m 1),[3] profilin (Cuc m 2),[4] and a pathogenesis-related protein belonging to the PR-1 family (Cuc m 3).[5]

A 40-year-old woman experienced ear and facial itching, followed by hives in her face, neck, thorax, and arms, and accompanied by dysphonia and shortness of breath 15 minutes after the intake of watermelon. One month later, she developed similar symptoms a few minutes after melon intake (toad skin variety). Both reactions were suitably resolved with intravenous antihistamines and corticosteroids at the emergency department, and no late response was observed. The patient had a previous history of oral itching after eating peach and fig but no symptoms with other fruits. One year later she reported episodes of oropharyngeal itching immediately after the intake of orange, banana, plum, and almond that had begun months earlier. The patient experienced rhinoconjunctivitis in the spring due to pollens and contact urticaria after touching dogs 2 years before her first visit.

The results of a skin prick test (SPT) to commercial melon extract (ME) were positive (positive control [histamine], 5 mm; negative control [saline], 0 mm), as were the results of prick-by-prick tests with melon (7 mm) and watermelon (6 mm). The total serum IgE level (UniCAP System; Phadia, Uppsala, Sweden) was 309 IU/mL, with a specific IgE level of 0.37 kU/L for melon and 0.52 kU/L for watermelon.

Lipid transfer proteins (LTPs) are proteins with high stability to thermal processing and digestion that typically induce systemic symptoms after ingestion.[6] Trying to identify the pattern of allergen sensitization in this patient, SPTs to profilins and a LTP marker (peach extract; ALK-Abelló, Madrid, Spain) were performed. The results of SPTs to melon profilin (Cuc m 2) isolated by López Torrejón et al[4] and palm pollen profilin (ALK-Abelló) were positive (5 and 14 mm, respectively), which confirmed the patient's sensitization to profilin, the major allergen in melon allergy in our area.[4] In contrast, the results of SPTs to peach peel extract (LTP marker) were negative, supporting the theory that the patient was not sensitized to LTP. Moreover, an allergenic LTP has not been identified in either melon or watermelon so far. The patient declined an oral provocation test with melon or watermelon when proposed.

Regarding other foods, the results of SPTs with nuts were also positive (wheal diameter, ≥3 mm) for peanut, chestnut, almond, sunflower seed, and pistachio, and the results of prick-by-prick tests were positive for orange and banana. SPTs of commercial common aeroallergens were performed with positive results for grass-pollen mix, *Olea europaea,* mugwort, *Chenopodium album,* plantain, dust mites, and cat and dog epithelium.

To search for potential allergens, we prepared ME and watermelon extract (WE) by homogenization in phosphate-buffered saline, dialysis, and lyophilization.[7] Potential allergenic components of ME and WE were detected by IgE immunodetection after sodium dodecyl sulfate–polyacrylamide gel electrophoresis separation (Figure 1A) using patient serum.[7] IgE-binding bands of approximately 55, 36, and 18 kDa were identified in both extracts (Figure 1B). Those bands from the ME were manually excised from the gel, digested with trypsin, and analyzed by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry and liquid chromatography–electrospray ionization tandem mass spectrometry.[7] Molecular characterization of IgE-binding bands was performed by mass spectrometry or tandem mass spectrometry, identifying the band of approximately 55 kDa as cucumisin (Cuc m 1), the band of approximately 36 kDa as malate dehydrogenase, and the band of approximately 18 kDa as phloem lectin Lec 17-1, when compared with the databases (Figure 1B). Malate dehydrogenase has recently been identified as a major allergen in watermelon allergy,[7] but it has never been described as an allergen in melon. Two lectins have been identified in melon (26 and 17 kDa),[8] but they have not been previously described as allergens in this fruit.

An additional band of 14 kDa was identified in the WE (Fig.1B), probably corresponding to profilin, but we failed to identify this band in the ME immunoblotting. We found no recognition when this ME was tested with an antiprofilin antibody,[4] probably because profilin is a labile protein and surely the level of allergen was insufficient for its detection by the specific antibody.

In summary, we describe a patient sensitized to profilin, cucumisin, malate dehydrogenase, and Lec 17-1, who was experiencing systemic reactions to melon and watermelon, which is an exceptional clinical manifestation for these fruits. Two of these proteins

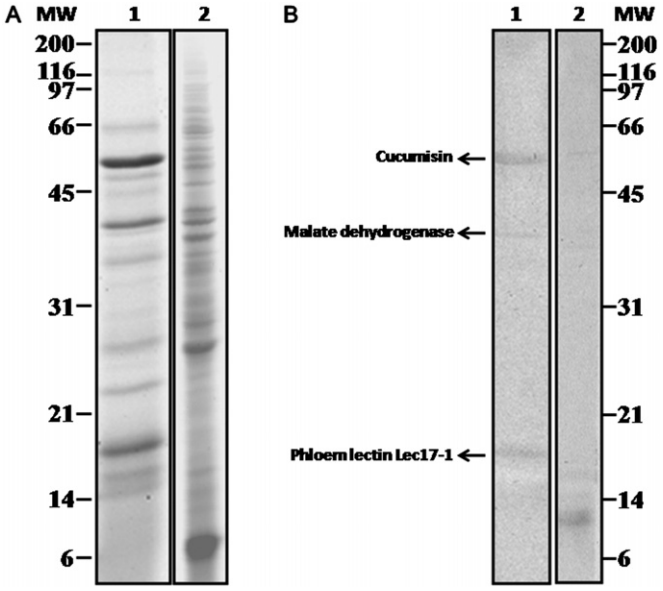


Figure 1. Identification of IgE-binding proteins in melon and watermelon extracts. A, Sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) after Coomassie Blue staining with the melon extract (line 1) and the watermelon extract (line 2). B, SDS-PAGE IgE immunoblotting with the melon extract (line 1) and the watermelon extract (line 2). MW indicates molecular weight marker.

**Disclosures:** Authors have nothing to disclose.



doi:10.1016/j.anai.2010.01.011

(malate dehydrogenase and phloem Lec 17-1) have been involved for the first time, to our knowledge, in melon allergy. It is also the first time, to our knowledge, that a lectin has been described as a potential allergen in the Cucurbitaceae family.

Eloina González-Mancebo, MD, PhD*
Gema López-Torrejón, PhD†
David González de Olano, MD*
Sara Santos, MD*
Mar Gandolfo-Cano, MD*
Amaya Meléndez*
Gabriel Salcedo, PhD†
Javier Cuesta-Herranz, MD, PhD‡
Fernando Vivanco, PhD§‖
Carlos Pastor-Vargas, PhD‖

*Unidad Alergia
Hospital de Fuenlabrada
†Unidad de Bioquímica
Departmento de BiotecnologíaETS Ingenieros Agrónomos
Universidad Politécnica
‡Departmento de Alergia
Fundación Jiménez Díaz
§Departmento de Inmunología
Fundación Jiménez Díaz
‖Departmento de Bioquímica y Biología Molecular I
Universidad Complutense
Madrid, Spain
egonzalez.hflr@salud.madrid.org

1. Figueredo E, Cuesta-Herranz J, De-Miguel J, et al. Clinical characteristics of melon (*Cucumis melo*) allergy. *Ann Allergy Asthma Immunol.* 2003;91:303–308.
2. Rodriguez J, Crespo JF, Burks W, et al. Randomized, double-blind, crossover challenge study in 53 subjects reporting adverse reactions to melon (*Cucumis melo*). *J Allergy Clin Immunol.* 2000;106:968–972.
3. Cuesta-Herranz J, Pastor C, Figueredo E, et al. Identification of Cucumisin (Cuc m 1), a subtilisin-like endopeptidase, as the major allergen of melon fruit. *Clin Exp Allergy.* 2003;33:827–833.
4. López Torrejón G, Crespo JF, Sanchez-Monge R, et al. Allergenic reactivity of the melon profilin Cuc m 2 and its identification as major allergen. *Clin Exp Allergy.* 2005;35:1065–1072.
5. Asensio T, Crespo JF, Sanchez-Monge R, et al. Novel plant pathogenesis-related protein family involved in food allergy. *J Allergy Clin Immunol.* 2004;114:896–899.
6. Salcedo G, Sanchez-Monge R, Barber D, Diaz-Perales A. Plant non-specific lipid transfer proteins: an interface between plant defence and human allergy. *Biochem Biophys Acta.* 2007;1771:781–791.
7. Pastor C, Cuesta-Herranz J, Cases B, et al. Identification of major allergens in watermelon. *Int Arch Allergy Immunol.* 2009;149:291–298.
8. Dinant S, Clark AM, Zhu Y, et al. Diversity of the superfamily of phloem lectins (Phloem Protein 2) in angiosperms. *Plant Physiol.* 2003;131:114–128.

## COMBINED CETIRIZINE-MONTELUKAST PREVENTIVE TREATMENT FOR FOOD-DEPENDENT EXERCISE-INDUCED ANAPHYLAXIS

Food-dependent exercise-induced anaphylaxis (FDEIA) appears during or soon after exercise if it is preceded by ingestion of foods, whereas food allergens and exercise are independently tolerated.[1] We describe a 17-year-old adolescent referred to us for 2 episodes of anaphylaxis that occurred while jogging on the beach 60 minutes after eating. Because of generalized urticaria, abdominal pain, vomiting, wheezing, dyspnea, and hypotension, he required hospitalization and emergency department treatment with epinephrine, intravenous antihistamine, and corticosteroids. His clinical history disclosed that on both occasions he had had milk for breakfast and a ham-cheese-tomato sandwich and peaches 1 hour before running.

The patient had seasonal rhinoconjunctivitis and took cetirizine (10 mg/d) whenever he had an attack. On admission, he underwent a physical examination and blood tests, the results of which were unremarkable. Basal serum tryptase levels (ImmunoCAP; Phadia, Uppsala, Sweden) were normal (2.96 ng/mL). Skin prick test results (Stallergenes, Antony, France) proved positive only to mites and grass pollen. Prick by prick with peach presented weak positivity (flare diameter, 10 mm; wheal diameter, 3 mm). IgE specific peach levels (ImmunoCAP) were 0.40 kUA/L.

Written consent was obtained from the patient and his parents. The boy started cetirizine therapy, with separate food challenges with milk, wheat, tomato, and peach being performed in a resting state. Results were negative. Ten-minute strenuous running tests were performed on a treadmill. No symptoms appeared after exercise tests performed in a fasting state. Open food-exercise challenges (OFECs) were performed 60 minutes after ingestion of the foods mentioned previously. Only the OFEC with 2 peaches was associated with generalized urticaria, nausea, swelling, coughing, and wheezing within 3 minutes. Symptoms quickly increased in intensity and were followed by vomiting and hypotension. After being treated with epinephrine, intravenous antihistamine, and corticosteroids, the patient showed progressive resolution of symptoms. His serum tryptase level after OFEC was high (18.02 ng/mL) but returned to the reference range within 48 hours.

Although there is a possibility that exercise challenges to diagnose FDEIA may not be completely reproducible, with negative challenge results alternating with positive results,[1] in this case report the positive OFEC confirmed a relationship between peach ingestion and symptoms. Because this was accompanied by increased tryptase serum concentrations, a double-blind exercise food challenge, the gold standard for FDEIA diagnosis,[1] was not considered necessary.

The patient and his parents expressed concern regarding other possible cross-reacting foods in the Rosaceae family and requested possible preventive treatment to be used in case of exercise shortly after ingesting potentially dangerous foods. Systemic reactions to peaches and apples in relation to sensitization to nonspecific lipid transfer proteins have been reported.[2] Because cetirizine alone was not effective, a trial with cetirizine (10 mg) plus montelukast (10 mg) daily for 3 days was prescribed to verify its preventive effect on FDEIA. Under pharmacological protection, the patient endured the entire test after OFECs with peaches and apples without any wheezing or symptoms. He was dismissed with a diagnosis of peach-induced FDEIA and was advised not to do strenuous exercise for at least 4 hours after eating peaches, to carry injectable epinephrine (Epipen; Dey LP, Napa, California) in case of an attack,[3] and to continue preventive therapy during the spring and summer consisting of cetirizine plus montelukast. He continued treatment as prescribed and did not experience any further episodes of FDEIA despite no limitations except peaches.

**Disclosures:** Authors have nothing to disclose.

doi:10.1016/j.anai.2009.12.002