Shin et al. World Allergy Organization Journal (2026) 19:101371
http://doi.org/10.1016/j.waojou.2026.101371

WORLD ALLERGY ORGANIZATION JOURNAL

Open Access

Profilin isoallergens, major but not immunodominant, from Korean melon

Yoon Ji Shin, BSc[a], Haeun Kim, BSc[a], Yong Seok Lee, PhD[b], Minkyu Sang, PhD[b], Kyunguk Jeong, MD, PhD[c], Sooyoung Lee, MD, PhD[c], Kyung Hee Park, MD, PhD[a], Jung-Won Park, MD, PhD[a] and Kyoung Yong Jeong, PhD[a]*

ABSTRACT

Background: Pollen food allergy syndrome (PFAS) is a common condition caused by cross-reactivity between pollen allergens and homologous proteins in certain fruits, vegetables, and nuts. Korean melon (*Cucumis melo* var. *makuwa*) is a frequent trigger of PFAS; however, its allergenic components have not been fully characterized.

Objective: This study aimed to identify the allergens responsible for PFAS in Korean melon and investigate potential differences in allergenic profiles among melon cultivars.

Methods: Allergen extracts from Korean melon were analyzed using proteomic and transcriptomic approaches. Profilin isoallergens (Cuc m 2.0102 and Cuc m 2.0301) were recombinantly expressed, and IgE reactivity was evaluated by ELISA and immunoblotting. Profilin content in melon extracts was quantified using targeted mass spectrometry.

Results: IgE immunoblotting of melon extracts revealed 3 allergenic components at approximately 60, 15, and 12 kDa. Proteomic analysis identified profilin (Cuc m 2) as the only allergen identified, whereas transcriptomic analysis additionally identified cucumisin (Cuc m 1) and pathogenesis-related protein 1 (PR-1; Cuc m 3). Two profilin isoallergens, Cuc m 2.0102 and Cuc m 2.0301, were identified, with Cuc m 2.0102 showing the highest identity to the canonical Cuc m 2.0101. Profilin abundance was lower in Korean melon than in other cultivars, including honeydew melon and Hami melon, and did not account for the majority of IgE reactivity. Inhibition assays further suggested that profilin is not the immunodominant allergen in patients with Korean melon. In contrast, sensitization to the 60 kDa allergen, a potential cucumisin (Cuc m 1), which was identified by transcriptomics, may reflect primary sensitization to Korean melon.

Conclusion: Profilin isoallergens Cuc m 2.0102 and 2.0301 were identified as major but not immunodominant allergens associated with PFAS in Korean melon. Variation in profilin content among melon cultivars suggests differences in allergenic potential. These findings contribute to the understanding of PFAS and may support the development of improved diagnostic approaches and allergen avoidance strategies.

Keywords: Pollen food allergy syndrome (PFAS), Korean melon, Profilin

[a]Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul, South Korea
*Corresponding author. Department of Internal Medicine, Yonsei University College of Medicine 50-1 Yonsei-ro, Seodaemun-gu, 03722, Seoul, South Korea. E-mail: jeongky@yuhs.ac
Full list of author information is available at the end of the article

http://doi.org/10.1016/j.waojou.2026.101371

Received 20 November 2025; Received in revised from 9 February 2026; Accepted 9 March 2026
Online publication date 30 March 2026

INTRODUCTION

Pollen Food Allergy Syndrome (PFAS), also referred to as Oral Allergy Syndrome (OAS), is the most common food allergy in adults. It occurs as a result of IgE cross-reactivity between pollen allergens and homologous proteins in certain raw fruits, vegetables, and nuts. Clinical manifestations are typically mild and confined to the oral cavity and pharynx; however, anaphylaxis has been reported, albeit rarely.

In Korea, the prevalence of PFAS was reported to be 41.7% in a nationwide study.[1] Among affected individuals, 8.9% experienced anaphylaxis. The most frequently implicated trigger foods were peach (48.5%), apple (46.7%), and kiwi (30.4%). In addition, several traditional foods, including taro (8.9%), ginseng (8.2%), perilla leaf (4.4%), and bellflower root (4.4%), were identified as causative foods. Despite their clinical relevance, the molecular characteristics of allergens derived from these foods have not been fully elucidated.[2] Korean melon was also identified as a frequent trigger, with a reported sensitization rate of 12.6%.

Pathogenesis-related protein 10 (PR-10) is recognized as a major allergen family responsible for PFAS.[3] The birch pollen allergen Bet v 1 serves as the prototype of this protein family, and in Korea, Que ac 1 from sawtooth oak is considered the primary sensitizing PR-10 allergen. Sensitization to tree pollen is associated with PFAS reactions to a wide range of plant-derived foods, including apple, pear, cherry, peach, hazelnut, peanut, carrot, celery, and soy.[4–6]

Profilin represents another panallergen implicated in PFAS. Allergy to raw melon, watermelon, citrus fruits, tomato, pineapple, persimmon, and banana has been described as a clinical marker of profilin sensitivity in patients with PFAS.[7] To date, 3 allergenic molecules from melon have been identified and registered by the Allergen Nomenclature Subcommittee (www.allergen.org): Cuc m 1 (cucumin), Cuc m 2 (profilin), and Cuc m 3 (PR-1).

Primary sensitization to grass, birch, ragweed, and mugwort pollen can lead to profilin hypersensitivity. Nevertheless, profilin is generally considered to play a limited role in respiratory allergic symptoms.[8] More recently, profilin has been proposed as a marker of disease severity and polysensitization in allergic individuals.[7]

Korean melon (*Cucumis melo makuwa*), also known as Oriental melon or chamoe in Korean, is a cultivar native to East Asia and is characterized by bright yellow skin with white longitudinal striped skin. It is widely consumed as a summer fruit in Korea. In a previous study, 12.6% of Korean patients with PFAS were sensitized to Korean melon, whereas the overall sensitization rate to melon was 11.5%.[1]

In this pilot study, we aimed to characterize the allergens responsible for PFAS associated with Korean melon. In addition, we sought to investigate potential differences in sensitization patterns between Korean melon and other melon cultivars in order to improve diagnostic accuracy.

MATERIAL AND METHODS

Serum samples

Serum samples were collected from 8 allergy patients (average age 16 years, range 5–24 years) who visited the Allergy-Asthma Center at Severance Hospital, Seoul, Korea (Table 1). These individuals had been diagnosed with PFAS based on immediate allergic reactions confirmed by allergists following ingestion of Korean melon or musk melon. Specific IgE levels to allergens were measured using ImmunoCAP (ThermoFisher Scientific, Uppsala, Sweden). Written informed consent was obtained from all participants prior to blood collection. The study was approved by the institutional review board of Yonsei University Health System (IRB no. 4-2022-0733).

Allergen extracts

Korean melon was purchased from a local market, and allergen extract was prepared from the flesh after removing the skin (rind) and seeds. The flesh was homogenized using a Waring blender in phosphate-buffered saline (PBS, pH 7.4). The extract was then centrifuged at 15,000 rpm at 4 °C for 30 min, and the supernatant was dialyzed (cutoff 10 kDa) against water, lyophilized, and stored at −20 °C. Protein concentration was determined using the Bradford

No.	Gender	Age	Diagnosis[a]	Comorbidity	Sensitization profile (kU_A/L)[b]	tIgE	Clinical history
1	M	22	PFAS		e1 (3), e5 (2)		Korean melon, peach, watermelon, apple, buckwheat, crab, *mosquito*
2	F	24	PFAS	AR			Korean melon, peach, plum, cherry, strawberry
3	F	19	PFAS	AR	f49 (3.63), f95 (17.10), T3 (>100), t7 (94.74), Tx9 (67.80)	1313	Korean melon, watermelon, tomato, apple, peach, kiwi
4	M	19	PFAS	AD		82	Korean melon, apple, pear, watermelon, citrus, strawberry
5	M	19	PFAS	AD, AR	Tx9 (41.10), T3 (44.00), T7 (53.60), Wx1 (16.70), f95 (10.20)	256	Korean melon, melon, apple, watermelon, pear, cucumber, banana, blueberry, pineapple, mango, mulberry, date
6	F	19	PFAS	AR	Tx9 (3.48), Wx1 (4.82)	873	Korean melon, melon, watermelon
7	F	5	PFAS		Tx9 (0.47), Wx1 (0.57)	169	Melon, peach
8	M	7	PFAS	AR	Tx9 (69.30), t3 (>100), t7 (79.60)	1126	Melon, watermelon, kiwi, banana

Table 1. Clinical features of enrolled patients. *[a]AD, atopic dermatitis; AR, allergic rhinitis; FA, food allergy; PFAS, pollen food allergy syndrome. [b]f49, apple; f95, peach; t2, grey alder; t3, birch; t4, hazel; t7, oak; t12, willow; tTx9, tree pollen mix (t2, t3, t4, t7, t12); w1, ragweed; w6, mugwort; w9, plantain; w10, goosefoot; w11; Russian thistle; wx1, weed pollen mix (w1, w6, w9, w10, w11)*

assay, and aliquots of the extract were stored at −70 °C until use.

Sugar melon, honeydew, and Hami melon extracts were obtained from DST Diagnostische Systeme & Technologien GmbH (Schwerin, Germany), and muskmelon was obtained from Stallergenes Greer International AG (Baar, Switzerland).

Identification of melon allergens by proteome analysis

Allergen extracts (Korean melon, 20 μg/well each) were separated by 15% SDS-PAGE and electroblotted onto a nitrocellulose membrane. After blocking with 3% skim milk in PBST, the membrane was incubated overnight with a pooled serum sample (1:4 dilution, from 2 patients who were positive for recombinant protein). IgE reactivity was detected using the same pooled serum (diluted 1:4), and IgE antibodies were visualized with alkaline phosphatase-conjugated goat anti-human IgE (1:1000; Sigma-Aldrich) for 1 h. Color development was initiated by adding nitro blue tetrazolium and 5-bromo-4-chloro-3-indolyl-phosphate (NBT/BCIP) (Promega, Madison, WI, USA).

For the identification of IgE-reactive components, LC-coupled ESI MS/MS analysis was performed following 2D gel electrophoresis and IgE immunoblotting.

Transcriptome analysis

Homologues of known allergens were identified by searching query sequences for Cuc m 1 (cucumisin), Cuc m 2 (profiling), and Cuc m 3 (PR-1) against subject sequences in the database using BLAST (BLASTX for proteins and BLASTN for nucleotides) at an E-value cutoff of e^{-5} (<0.00001).[9] Gene ontology (GO) analysis was conducted using the BLAST2GO professional software (http://www.BLAST2go.org/) based on PANM DB annotation, and unigenes were classified into GO term categories (level 2) using WEGO software (http://wego.genomics.org.cn/cgi-bin/wego/index.pl/).[10]

Expression and purification of recombinant profilin isoforms (Cuc m 2.0102 and 2.0301)

cDNA sequences encoding the profilin isoallergens Cuc m 2.0102 and Cuc m 2.0301 were synthesized and ligated into the pBT7-N-His expression vector (Bioneer, Daejeon, Korea). The plasmids were transformed into *Escherichia coli* Rosetta 2 cells, and recombinant protein production was induced by adding 1 mM isopropyl β-D-1-thiogalactopyranoside (IPTG). The proteins were purified using Ni-affinity column chromatography.

Assessment of IgE reactivity

Recombinant proteins (2 μg/mL) were coated onto microplates and incubated overnight at 4 °C. After blocking with 3% skim milk in PBST, serum samples (diluted 1:4 in PBST containing 1% bovine serum albumin [BSA]) were added and incubated for 1 h at room temperature. Allergen-specific IgE antibodies were probed with biotinylated goat anti-human IgE (1:1000, Vector, Burlingame, CA, USA), and streptavidin-horseradish peroxidase (1:1000, Sigma-Aldrich, St. Louis, MO, USA). Color development was initiated by adding 3,3′,5,5′-tetramethyl-benzidine (TMB) substrate (SeraCare Life Sciences, Milford, MA, USA), and absorbance at 450 nm was measured. A cutoff value was determined by calculating the mean absorbance plus 2 standard deviations of sera from healthy controls.

For inhibition assays, 10 μg of Korean melon extract was coated onto a microplate. A pooled serum sample was incubated with various concentrations of recombinant profilins for 2 h at room temperature, followed by overnight incubation at 4 °C. The remaining steps were performed as described above. The percentage of inhibition was calculated using formula $(1-A_i/A_0) \times 100$, where A_i represents absorbance with the inhibitor and A_0 represents absorbance without the inhibitor.

Quantification of profilin isoforms by MRM mass spectrometry

Target peptides for Cuc m 2.0102 (DGSVWAQSQNFPQLKPEEVAGIVG, GNHLTSA AIIG, DGSVWAQSQNFPQLKPE, and GPGGVTVK) and for Cuc m 2.0301 (DFDEPGSLAPTGLHLGGSK and GTSGITVK) were selected using Skyline software (www.skyline.ms), and synthetic peptides were produced (>97% purity). Targeted multiple reaction monitoring (MRM) mass spectrometry was performed using a TQ 6500+ Mass

Spectrometer (AB SCIEX Korea Ltd, Daejeon, Korea) coupled with micro-nano dual liquid chromatography (Eksigent Technologies LLC, Newark, DE, USA). Calibration curves were generated with 8 different concentrations of peptides (2-fold serial dilutions from 50 nM) with triplicate analyses. Results with an r^2 above 0.99 were accepted for further analysis. The coefficient of variation (CV), limit of detection (LOD), and limit of quantification (LOQ) were calculated to assess linearity and reproducibility. LOD was calculated as $3.3 \times \sigma/s$, where σ is the standard deviation (SD) of the peak area from blank analysis, and s is the gradient of the calibration curve. LOQ was defined as $10 \times \sigma/s^2$. For sample preparation, tryptic-digested extracts were desalted with SOLA HRP well plate C18 cartridges (Thermo Fisher Scientific) and dried using SpeedVac (Thermo Fisher Scientific). Quantification of Cuc m 2.0102 was optimized using the peptide GPGGVYVK ($r^2 = 0.9993$, lower LOQ = 0.39063 nM, upper LOQ = 50.000 nM), and DFDEPGSLAPTGLHLGGSK ($r^2 = 0.9982$, lower LOQ = 8.350 nM, upper LOQ = 267.192 nM) was used for Cuc m 2.0301 quantification, ensuring reproducibility and accuracy within the low and upper detection limits.

RESULTS

Putative allergens identified by transcriptomic analysis

Three potential allergen candidates were identified through RNA sequencing analysis. A sequence (Cm_Uni_010942) showed 40.1% sequence identity to cucumisin (Cuc m 1), while another sequence (Cm_Uni_013173) shared 27.2%–29.3% identity with PR-1 allergens: 29.3% to Cuc m 3, 29.2% to Pru p 9, 27.2% to Art v 2, and 28.1% to Cyn d 24 (Table 2). Two distinct profilin isoallergens were also identified: Cuc m 2.0102 (Cm_Uni_034003) shares 99.2% identity with Cuc m 2.0101, while Cuc m 2.0301 (Cm_Uni_022908) shares 72.5% identity with Cuc m 2.0101. Cuc m 2.0102 exhibited 69.2% (mugwort allergen Art v 4, ragweed allergen Amb a 8) to 89.3% (watermelon allergen Citr l 2) sequence identity, and Cuc m 2.0301 exhibited 66.2% (Amb a 8) to 83.2% (walnut allergen Jug r 7) identity (Fig. 1). Cuc m 2.0102 and 2.0301 share 72.5% sequence identity. Cuc m 2.0102 was deposited in GenBank under accession No. PX514932 and Cuc m 2.0301 under PX514933.

Identification of profilin allergen by proteomic analysis

Melon extracts from 5 different cultivars were analyzed to identify allergenic components. The 5 extracts exhibited distinct protein banding patterns. Bands about 50, 20, and 15 kDa were common across all extracts (Fig. 2). Notably, a thick band near the well was observed in the sugar melon extract. In IgE immunoblotting, bands around 60, 15, and 12 kDa were prominent, although their intensities varied. These bands correspond to Cuc m 1 (67 kDa cucumisin), Cuc m 3 (17 kDa PR-1), and Cuc m 2 (14 kDa profilin). Strong IgE reactivity to the 60 kDa protein was observed in Korean, honeydew, and Hami melons, while IgE reactivity to the 15 and 12 kDa bands was most prominent in sugar and musk melons.

Proteomic analysis was conducted to further investigate these proteins. Six IgE-reactive spots from 2D gels were selected for tandem MS analysis. Profilin was the only protein identified with a meaningful mascot score (65). The identification of other allergens may have been hindered by post-translational modifications or the low concentration of proteins. Therefore, recombinant profilin isoallergens Cuc m 2.0102 and 2.0301 were produced. Notably, spot 1, with a molecular weight of approximately 60 kDa, showed strong IgE reactivity.

Allergenicity of profilin isoallergens

Recombinant proteins for both isoallergens, Cuc m 2.0102 and Cuc m 2.0301, were successfully produced (Fig. 3). IgE reactivity to both isoallergens was indistinguishable (correlation coefficient, $\rho = 0.999183$). Both allergens were recognized by 62.5% (5/8) of IgE antibodies from Korean melon and/or melon-related PFAS. Specifically, 50% (3/6) of Korean melon allergy patients and 75% (3/4) of melon allergy patients tested positive for profilin allergens.

Biochemical identity	Allergen	Species	Sequence identity	Sequence number	QueryID
Alkaline serine protease (cucumisin) <67 kDa>	Cuc m 1	Muskmelon (*Cucumis melo*)	40.1%	28	Cm_Uni_008068, Cm_Uni_012133, Cm_Uni_002455, Cm_Uni_020604, Cm_Uni_038234, Cm_Uni_017369, Cm_Uni_024571, Cm_Uni_041480, Cm_Uni_038234, Cm_Uni_013657, Cm_Uni_008485, Cm_Uni_012920, Cm_Uni_024922, Cm_Uni_038050, Cm_Uni_042102, Cm_Uni_016632, Cm_Uni_010942, Cm_Uni_010943, Cm_Uni_014762, Cm_Uni_018161, Cm_Uni_042278, Cm_Uni_009995, Cm_Uni_020604, Cm_Uni_011204, Cm_Uni_033014, Cm_Uni_000429, Cm_Uni_023427, Cm_Uni_038823
Profilin (Cuc m 2.0102)	Cuc m 2	Muskmelon (*Cucumis melo*)	99.2%	4	Cm_Uni_041161, Cm_Uni_034003, Cm_Uni_034002, Cm_Uni_022908
	Ana c 1	Pineapple (*Ananas comosus*)	76.3%		
	Citr l 2	Watermelon (*Citrullus lanatus*)	89.3%		
	Cit s 2	Sweet orange (*Citrus sinensis*)	76.3%		
	Fra a 4	Strawberry (*Fragaria ananassa*)	87.8%		
	Mal d 4	Apple (*Malus domestica*)	77.1%		
	Mus a 1	Dwarf banana (*Musa acuminata*)	77.1%		
	Ara h 5	Peanut (*Arachis hypogaea*)	79.4%		
	Jug r 7	English walnut (*Juglans regia*)	80.2%		
	Zea m 12	Maize (*Zea mays*)	77.9%		
	Cap a 2	Bell pepper (*Capsicum annuum*)	84.7%		

	Dau c 4	Carrot (*Daucus carota*)	82.14%		
	Amb a 8	Ragweed (*Ambrosia artemisiifolia*)	69.2%		
	Art v 4	Mugwort (*Artemisia vulgaris*)	69.2%		
	Cyn d 12	Bermuda grass (*Cynodon dactylon*)	80.2%		
	Bet v 2	Birch (*Betula pendula*)	74.4%		
	Que ac 2	Sawtooth oak (*Quercus acutissima*)	75.2%		
Profilin (Cuc m 2.0301)	Cuc m 2	Muskmelon (*Cucumis melo*)	72.5%	4	Cm_Uni_041161, Cm_Uni_034003, Cm_Uni_034002, Cm_Uni_022908
	Ana c 1	Pineapple (*Ananas comosus*)	74.8%		
	Citr l 2	Watermelon (*Citrullus lanatus*)	74.1%		
	Cit s 2	Sweet orange (*Citrus sinensis*)	73.3%		
	Fra a 4	Strawberry (*Fragaria ananassa*)	77.1%		
	Mal d 4	Apple (*Malus domestica*)	73.3%		
	Mus a 1	Dwarf banana (*Musa acuminata*)	75.6%		
	Ara h 5	Peanut (*Arachis hypogaea*)	72.5%		
	Jug r 7	English walnut (*Juglans regia*)	83.2%		
	Zea m 12	Maize (*Zea mays*)	72.5%		

(continued)

Biochemical identity	Allergen	Species	Sequence identity	Sequence number	QueryID
	Cap a 2	Bell pepper (*Capsicum annuum*)	77.1%		
	Dau c 4	Carrot (*Daucus carota*)	76.1%		
	Amb a 8	Ragweed (*Ambrosia artemisiifolia*)	66.2%		
	Art v 4	Mugwort (*Artemisia vulgaris*)	66.9%		
	Cyn d 12	Bermuda grass (*Cynodon dactylon*)	73.3%		
	Bet v 2	Birch (*Betula pendula*)	72.9%		
	Que ac 2	Sawtooth oak (*Quercus acutissima*)	75.9%		
Pathogenesis-related protein 1	Cuc m 3	Muskmelon (*Cucumis melo*)	29.3%	1	Cm_Uni_013173
	Pru p 9	Peach (*Prunus persica*)	29.2%		
	Art v 2	Mugwort (*Artemisia vulgaris*)	27.2%		
	Cyn d 24	Bermuda grass (*Cynodon dactylon*)	28.1%		

Table 2. (Continued) Allergen homologues from Korean melon transcriptomes

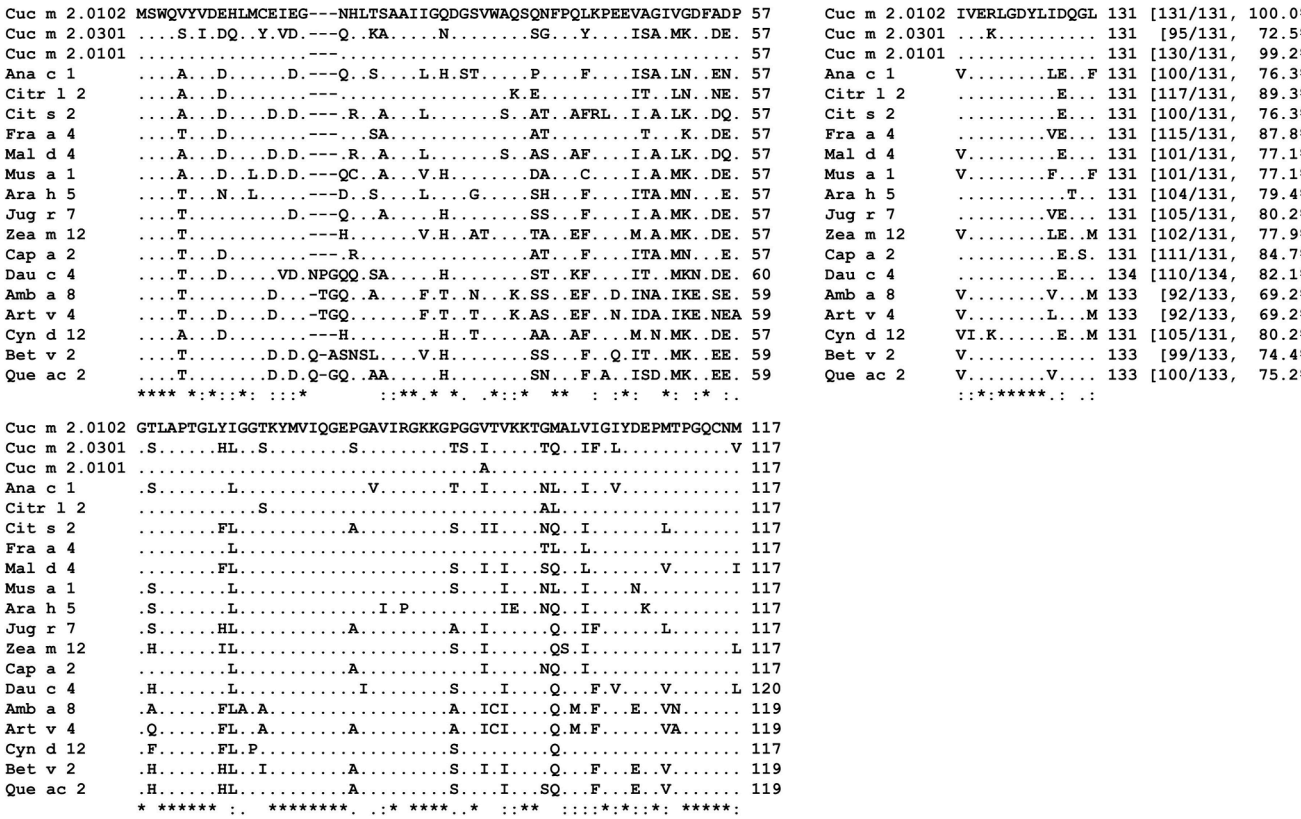

Fig. 1 Sequence alignment of Korean melon profilin isoallergens Cuc m 2.0102 and Cuc m 2.0301 with allergenic profilins. Cuc m 2.0102 (Korean melon, *Cucumis melo* var. makuwa, Access No. PX514932), Cuc m 2.0301 (Korean melon, PX514933), Cuc m 2.0101 (muskmelon, *Cucumis melo*, AAW69549), Ana c 1 (pineapple, *Ananas comosus*, AAK54835), Citr l 2 (Watermelon, *Citrullus lanatus*, AAU43733), Cit s 2 (sweet orange, *Citrus sinensis*, CAI23765), Fra a 4 (Strawberry, *Fragaria ananassa*, XP_004287490), Mal d 4 (apple, *Malus domestica*, AAD29414), Mus a 1 (dwarf banana, *Musa acuminata*, AAK54834), Ara h 5 (peanut, *Arachis hypogaea*, AAD55587), Jug r 7 (English walnut, *Juglans regia*, AVD53651), Zea m 12 (Maize, *Zea mays*, CAA51718), Cap a 2 (bell pepper, *Capsicum annuum*, CAD10376), Dau c 4 (carrot, *Daucus carota*, AAL76933), Amb a 8 (common ragweed, *Ambrosia artemisiifolia*, AAX77687), Art v 4 (mugwort, *Artemisia vulgaris*, CAD12861), Cyn d 12 (Bermuda grass, *Cynodon dactylon*, CAA69670), Bet v 2 (European white birch, *Betula pendula*, AAA16522), Que ac 2 (sawtooth oak, *Quercus acutissima*, QVU02258)

Both isoallergens inhibited less than 20% of IgE reactivity to the Korean melon extract, while 76.3% self-inhibition was observed.

Profilin content in 5 different melon cultivars

Profilin content was measured in extracts from 5 different melon cultivars using target peptides specific to each isoallergen (Table 3). Profilin content was approximately 92 times higher in sugar melon (16.52 μg/mL) compared to muskmelon (0.18 μg/mL). Interestingly, Cuc m 2.0301 was detected in Korean and sugar melons, whereas Cuc m 2.0102 was detected in all 5 cultivars.

DISCUSSION

Strict allergen avoidance, including avoidance of cross-reactive allergen sources, is the primary strategy for managing food allergies. However, unnecessary or overly restrictive avoidance of culprit foods may lead to nutritional deficiencies.[11] Therefore, distinguishing foods that can be safely consumed from those that may elicit allergic reactions is essential. A better understanding of allergenic components in homologous foods and their cross-reactivity may help allergists and patients make informed dietary decisions. Several melon cultivars are commercially available, and profilin in Korean melon has been considered one of the causative allergens of PFAS, which is characterized by cross-reactivity between pollen allergens and certain plant-derived foods.[12] Profilin is a well-known pan-allergen and a major allergen in melon, with a highly conserved conformational IgE epitope identified in Cuc m 2, explaining its broad cross-reactivity with pollen profilins.[13,14]

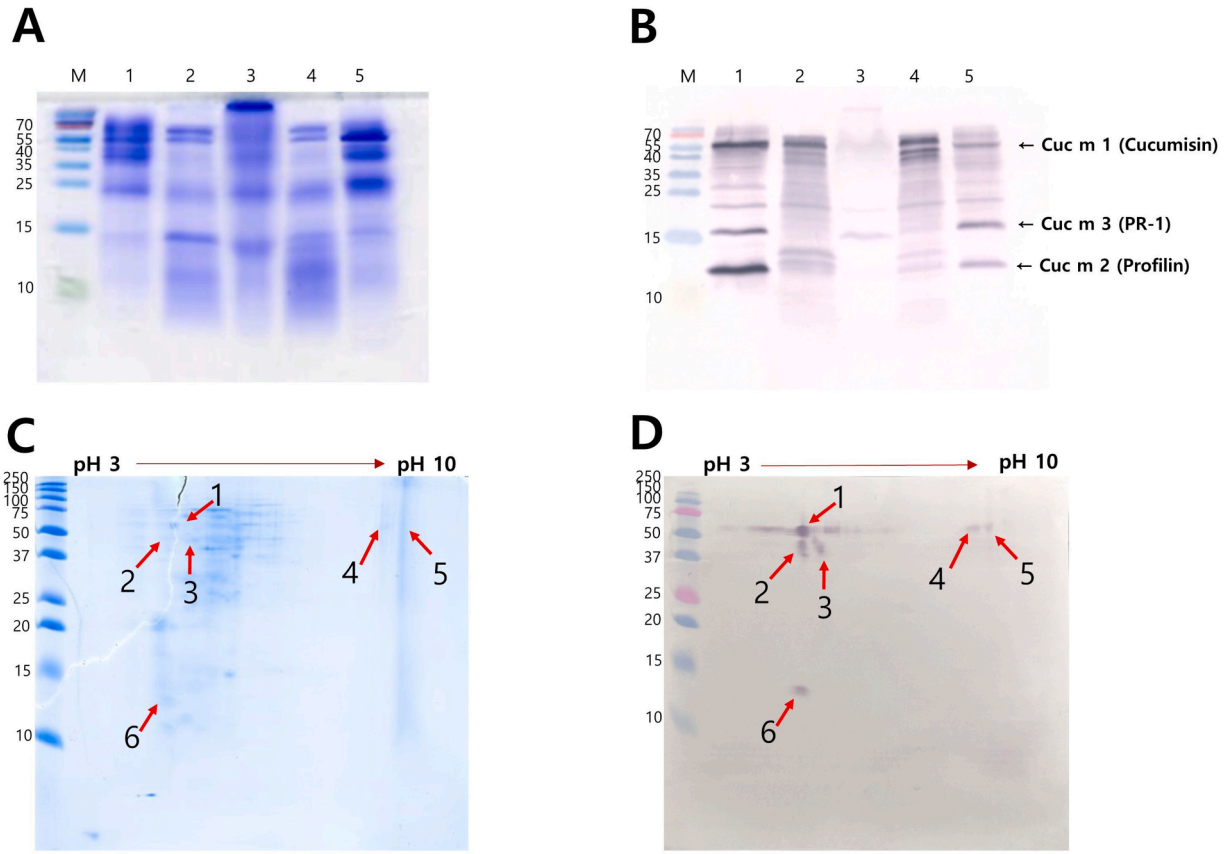

Fig. 2 Identification of IgE reactive components from Korean melon. SDS-PAGE analysis of the extracts from 5 different melon cultivars (A). IgE reactive components probed with IgE antibodies from patient sera (B). 2 D gel analysis of Korean melon extract (C). IgE reactive proteins were probed with serum IgE antibodies (D). M, molecular mass standard; 1, Korean melon; 2, honeydew melon; 3, sugar melon; 4, Hami melon; 5, muskmelon

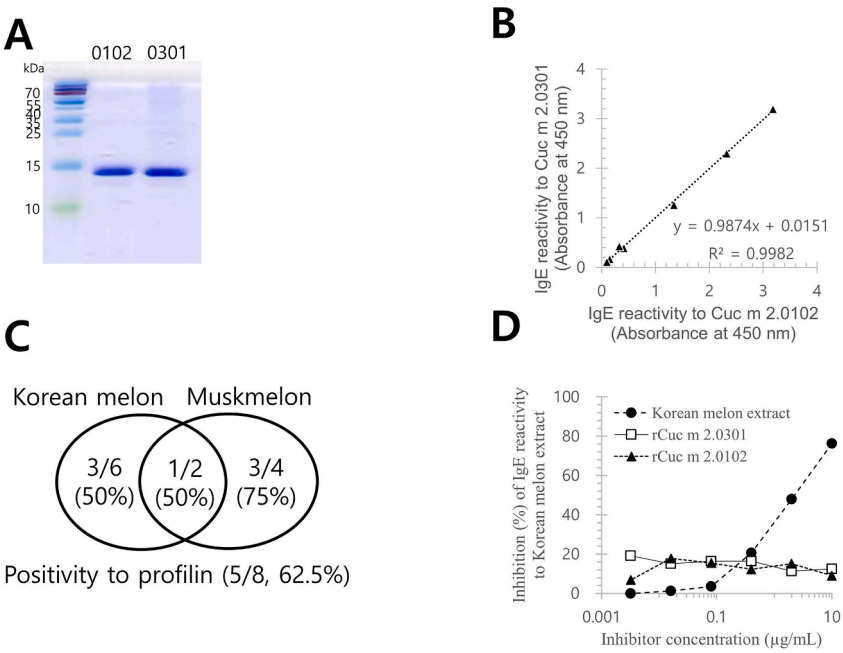

Fig. 3 IgE reactivity of recombinant profilin isoallergens, Cuc m 2.0102 and 2.0301. SDS-PAGE analysis of purified allergens (A). IgE reactivity of recombinant Cuc m 2.0102 and 2.0301 (B). IgE positivity to profilin from Korean melon and/or melon allergic patients (C). Inhibition analysis of recombinant profilins on Korean melon extract (D)

Common name	Scientific name (cultivar)	Profilin content MRM (ng/μg)		Profilin content (ng/μg) MRM
		34003 (2.0102)	22908 (2.0301)	
Korean melon (chamoe)	*Cucumis melo* var. *makuwa*	0.64	1.073	1.713
Musk melon	*Cucumis melo* L.	0.18	ND	0.18
Sugar melon	*Cucumis melo* var. *reticulates*	1.74	1.632	3.372
Honeydew melon	*Cucumis melo* L. (Inodorus group)	16.52	ND	16.52
Hami melon	*Cucumis melo* var. *saccharinus*	14.85	ND	14.85

Table 3. Profilin content in 5 different melon cultivars. *ND, not determined (probably below the detection limit)*

In this pilot study, we aimed to characterize allergens responsible for PFAS associated with Korean melon. At least 3 distinct IgE-reactive components, with approximately 60, 15, and 12 kDa, were detected. However, proteomic analysis identified profilin (Cuc m 2) as the only allergen, whereas transcriptomic analysis revealed sequences homologous to cucumisin (Cuc m 1; 40.1% identity) and PR-1 (Cuc m 3; 27.2–29.3% identity). Thus, we focused on the profilin allergen.

Two profilin isoallergens, Cuc m 2.0102 and Cuc m 2.0301, were identified from Korean melon. Cuc m 2.0102 shared 99.2% identity with the canonical Cuc m 2.0101, whereas Cuc m 2.0301 shared 72.5% identity. We investigated whether sensitization to Korean melon could be differentiated from other melon cultivars using profilin isoallergens. However, the 2 isoallergens were indistinguishable in terms of allergenicity and IgE-binding specificity.

Although profilin did not account for dominant IgE reactivity to Korean melon extract, quantitative analysis using MRM mass spectrometry revealed substantial differences in profilin content among melon cultivars. Honeydew and Hami melons exhibited high profilin concentrations, whereas Korean melon, the most commonly consumed cultivar in Korea, and muskmelon contained relatively low amounts of profilin. Consistent with this finding, cantaloupe melon profilin has been reported at 11.83 ng/g of fruit pulp using monoclonal antibody-based ELISA, which is markedly lower than the reported concentration of banana profilin (373.24 ng/g).[15]

Despite its low profilin content – approximately 92-fold lower than that of sugar melon - Korean melon remains a frequent trigger of PFAS. This observation supports the hypothesis that allergens other than profilin may play a primary role in Korean melon-associated allergy.

Inhibition ELISA further indicated that profilin is not the immunodominant allergen in patients with Korean melon allergy. Sensitization to pollen profilin and PR-1 may contribute to PFAS, which is consistent with the relatively low sensitization rate to grass pollen, in which profilin is the major allergen.[16] However, a strong IgE-reactive band at approximately 60 kDa band was consistently observed in immunoblot analyses. Sensitization to this 60 kDa protein, a putative major allergen candidate, may reflect primary sensitization to Korean melon and could serve as a potential marker for such cases. Further studies are therefore warranted to characterize this allergen in greater detail.

Determining whether primary sensitization to Korean melon is prevalent remains an important unanswered question. Distinguishing patients primarily sensitized to pollen from those primarily sensitized to Korean melon could substantially improve diagnostic accuracy, particularly if the 60 kDa allergen can be fully identified and characterized.

A protein of approximately 60 kDa, possibly cucumisin, was detected predominantly in Korean melon and represents a plausible candidate for primary sensitization. Multiple molecular forms of cucumisin, including the 67 kDa native form, the 54 kDa mature form, and a 36 kDa N-terminal fragment, have been detected.[17]

This study has several limitations. The small sample size limits the generalizability of the findings, and future studies including larger patient cohorts are required. In addition, the identities of the 60 and 12 kDa IgE-reactive proteins could not be conclusively determined, primarily due to the limited availability of patient serum samples.

In conclusion, we identified the profilin isoallergens Cuc m 2.0102 and 2.0301 from Korean melon as contributing allergens associated with PFAS. Differences in profilin content among 5 melon cultivars suggest variable allergenic potential. Further investigation into primary sensitization to Korean melon may advance allergen characterization, improve diagnostic precision, and inform more targeted allergen avoidance strategies.

Abbreviations
PFAS, pollen-food allergy syndrome; PR-10, pathogenesis-related 10; nsLTP, non-specific lipid transfer protein; ELISA, Enzyme-linked immunosorbent assayMS/MS tandem mass spectrometry; SDS-PAGE; sodium dodecyl sulfate-polyacrylamide gel electrophoresis; PBS, phosphate buffered saline; PBST, PBS containing 0.5% Tween 20; NBT, nitro blue tetrazolium; BCIP, 5-bromo-4-chloro-3-indolyl-phosphate; MRM, multiple reaction monitoring; TMB, 3,3′5,5′-tetramethyl-benzidine; IPTG, isopropyl-b-D-thiogalactopyranoside; IgE, immunoglobulin E

Funding
This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. 2022R1A2C100418411).

Data availability statement
The data that support the findings of this study are available from the corresponding author upon request.

Author contributions
KY Jeong performed purification and cloning. MK Sang and YS Lee analyzed transcriptomes. YJ Shin examined IgE reactivity. KH Park and JW Park collected serum samples. KY Jeong and JW Park designed the study. KH Park and KY Jeong wrote the manuscript.

Authors' consent for publication
All authors read and approved the final version of the manuscript and gave final consent for publication in WAO Journal.

Declaration of competing interest
KY Jeong reports a research grant from the National Research Foundation of Korea (NRF). JW Park reports being an unpaid chief technology officer for Prolagen Ltd. The authors (KY Jeong, and JW Park, and KH Park) own stocks in Prolagen Ltd. At the same time, KY Jeong, and JW Park also hold shares in Protia Ltd., Patents have been issued for the allergenic molecules Cuc m 2.0201. The reported conflict of interest did not influence academic integrity in analyzing data and writing a paper.

Disclosure of the use of generative AI and AI-assisted technologies in the writing process
Nothing to disclose.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2026.101371.

Author details
[a]Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul, South Korea. [b]Department of Biology, Soonchunhyang University, Asan, South Korea. [c]Department of Pediatrics, Ajou University, Suwon, South Korea.

REFERENCES

1. Kim MA, Kim DK, Yang HJ, et al. Pollen-food allergy syndrome in Korean pollinosis patients: a nationwide survey. *Allergy Asthma Immunol Res*. 2018;10(6):648–661.
2. Jeong KY, Park JW. Neglected but clinically relevant allergens in Korea. *Curr Allergy Asthma Rep*. 2024;24(9):519–526.
3. Poncet P, Sénéchal H. Charpin. Update on pollen-food allergy syndrome. *Expert Rev Clin Immunol*. 2020;16(6):561–578.
4. Jeong KY, Son M, Park JH, et al. Cross-reactivity between oak and birch pollens in Korean tree pollinosis. *J Kor Med Sci*. 2016;31(8):1202–1207.
5. Jeong KY, Lee J, Yuk JE, et al. Characterization of the major allergen, Que ac 1, from sawtooth oak pollen. *Allergy*. 2021;76(8):2626–2629.
6. Jeong KY, Park JW. Oak pollen allergy in Korea. *Curr Protein Pept Sci*. 2022;23(11):721–730.
7. Rodríguez Del Río P, Díaz-Perales A, Sánchez-García S, et al. Profilin, a change in the paradigm. *J Investig Allergol Clin Immunol*. 2018;28(1):1–12.
8. Asero R, Jimeno L, Berber D. Preliminary results of a skin prick test-based study of the prevalence and clinical impact of hypersensitivity to pollen panallergens (profilin and polcalcin). *J Investig Allergol Clin Immunol*. 2010;20:35–38.
9. Camacho C, Coulouris G, Avagyan V, et al. BLAST+: architecture and applications. *BMC Bioinf*. 2009;10:421. https://doi.org/10.1186/1471-2105-10.
10. Ye J, Fang L, Zheng H, et al. WEGO: a web tool for plotting GO annotations. *Nucleic Acids Res*. 2006;34:W293–W297.
11. Durban R, Groetch M, Meyer R, et al. Dietary management of food allergy. *Immunol Allergy Clin*. 2021;41(2):233–270.

12. Fugueredo E, Cuesta-Herranz J, D-Miguel J, et al. Clinical characteristics of melon (*Cucumis melo*) allergy. *Ann Allergy Asthma Immunol*. 2003;91:303–308.

13. Tordesillas L, Pacios LF, Palacín A, Cuesta-Herranz J, Madero M, Dıaz-Perales A. Characterization of IgE epitopes of Cuc m 2, the major melon allergen, and their role in cross-reactivity with pollen profilins. *Clin Exp Allergy*. 2009;40:174–181.

14. Tordesillas L, Gamboa P, Sanz ML, et al. A mutant of the major melon allergen, Cuc m 2, with reduced IgE binding capacity is a good candidate for specific immunotherapy. *Mol Immunol*. 2011;49:504–511.

15. Abdedini S, Sankian M, Falak R, Tehrani M, Talebi F, Shirazi FG. An approach for detection and quantification of fruits' natural profilin: natural melon profiling as a model. *Food Agric Immunol*. 2011;22:47–55.

16. Asero R, Tripodi S, Dondi A, et al. Prevalence and clinical relevance of IgE sensitization to profilin in childhood: a multicenter study. *Int Arch Allergy Immunol*. 2015;168(1):25–31.

17. 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(6):827–833.