REVIEW

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Exploring geographical variances in component-resolved diagnosis within the Asia-Pacific region

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Editor: Ömer Kalayci

Abstract

Component-resolved diagnostics (CRD) have revolutionized allergy diagnosis, offering enhanced accuracy and insights into allergen sensitization patterns. This review explores geographical variances in CRD for food and aeroallergens across the Asia-Pacific region. We examine the varying prevalence of allergic diseases and the utility of CRD in diagnosing common food allergies, including peanut, shellfish, fish, wheat, and fruits. Notable differences in serum-specific (sp)IgE sensitization patterns and the clinical relevance of particular allergen components are observed between populations in Asian countries and those in Europe and the United States. For food allergies, the literature reports significant differences in allergen components and their diagnostic utility across various countries. Peanut allergy diagnostics, particularly Ara h 2 splgE, show varying sensitivity and specificity between Asian and Western populations. In shellfish allergy, emerging allergens beyond tropomyosin are gaining importance in the Asia-Pacific region. Fish and wheat allergies also demonstrate unique sensitization patterns, emphasizing the need for region-specific diagnostic approaches. Regarding aeroallergens, pollen sensitization profiles vary widely across the

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; AUC, area under the curve; CCDs, cross-reactive carbohydrate determinants; CRD, component-resolved diagnostics; GAN, Global Asthma Network; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; HWP-WDEIA, WDEIA with reactions to hydrolyzed wheat protein; ISAAC, International Study of Asthma and Allergies in Childhood: LFS, Latex-fruit syndrome: LTP, lipid transfer protein: OAS, oral allergy syndrome: PFAS, pollen food allergy syndrome: SCP, sarcoplasmic calcium-binding protein; splgE, serum specific IgE; SPT, skin prick tests; WDEIA, wheat-dependent exercise-induced anaphylaxis; ω5G, omega-5 gliadin.

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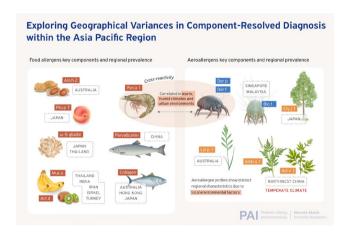
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region, influenced by local flora and climate, to influence symptoms of pollen food allergy syndrome. House dust mite allergens remain a significant concern, with high sensitization rates to major components like Der p 1, Der p 2, and the emerging Der p 23. The cross-reactivity between house dust mite and shellfish allergens is particularly relevant in this region. These findings emphasize the need for region-specific CRD approaches, considering local allergen profiles and sensitization patterns. As the prevalence of allergic diseases continues to rise in the Asia-Pacific, further research into locally relevant allergens and their components is crucial for improving diagnosis, patient management, and targeted immunotherapy strategies in this diverse region.

KEYWORDS

Asia-Pacific, component-resolved diagnosis, geographical variance, molecular allergology



1 | INTRODUCTION

Component-resolved diagnostics (CRD) are increasingly becoming a part of the allergist's toolkit. CRD involves analyzing serum specific (sp) IgE levels directed against individual allergenic proteins or components rather than whole allergen extracts. In many cases, CRD offers greater diagnostic accuracy than traditional skin prick tests or spIgE to whole allergens, such as Ara h 2 and Ana o 3 for peanut and cashew allergies, respectively. 1-5 Given the known variations in allergens and allergy prevalence observed in the epidemiological literature worldwide, considering the range of allergens specific to the Asia-Pacific region is important for the accurate diagnosis and management of allergic diseases. This review considers geographical variances in CRD for food and aeroallergens in the Asia-Pacific Region.

2 | DIFFERENCE IN PREVALENCE OF ALLERGIC DISEASE ACROSS ASIA-PACIFIC REGION

Although allergies were once thought to be rare in Asia, recent evidence suggests that they are becoming more common. Survey data indicates that the prevalence of food allergy in Taiwan has increased

from 7.7% to 10.4% in children and from 6.4% to 12.5% in adults, between 2004 and 2017.6 In the Chongging region of China, food allergy, confirmed using oral food challenges, increased from 3.5% in 1999 to 7.7% in 2009 and 11.1% in 2019. This rise mirrors global trends. For example, in Australia, which has one of the highest food allergy rates worldwide, approximately 10% of children have food allergies, including a 3% prevalence of peanut allergy. 8 Similarly, in the United States, 7.6% of children have food allergies, with shellfish allergy being particularly common. The triggers of food allergy vary between regions, with seafood allergies being more common in Southeast Asia, while wheat allergies are more common in Japan and Thailand. 10,11 Egg, milk and seafood are among the most common food allergies in China. 12 In contrast, peanut and tree nut allergies are more prevalent in urbanized regions like Australia and Singapore. 13,14 Migration from Asia to Australia also influences the prevalence of allergic disease, with babies living in Australia born to Asian parents exhibiting a higher prevalence of food allergy compared to infants living in Australia with Australian-born parents. 15

A recent systematic review found that the prevalence of allergic rhinitis (AR) varies greatly depending on the region and method of defining the outcome, ranging from 1.0% to 47.9% for Asia and 19.2% to 47.5% for Oceania. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three survey involving 61 countries showed that 6.9% of

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adolescents worldwide experienced severe asthma symptoms, including 3.8% of those in Asia-Pacific and Northern and Eastern Europe and 11.3% in North America. ¹⁷ Although the prevalence of asthma in the Asia-Pacific region was comparatively lower compared to that in Western countries, including Australia, where the prevalence of AR is 23.8% (NHS survey 2023), recent evidence shows that the prevalence is on the rise, particularly in countries with rapidly developing economies, such as China. ¹⁸

A cross-sectional study conducted across 18 countries found that the prevalence of atopic dermatitis (AD), based on the ISAAC criteria and self-report of AD diagnosis, was between 2.7% and 20.1%; the prevalence of AD was around 11% in Japan and Taiwan. ¹⁹ The Global Asthma Network (GAN) assessed eczema prevalence and severity across 27 global centers over time. ²⁰ The study found only a small overall 10-year increase in both current eczema and severe eczema prevalence, with no significant increase in Asia. However, there was substantial variation between centers, even within the same income group, highlighting that while income level helps explain some regional patterns, it does not fully account for the observed differences in eczema prevalence globally. Other factors, such as geography, climate, environment, urbanization, and cultural practices, likely play crucial roles. These differences underscore the importance of region-specific studies and tailored strategies to manage allergies effectively in the Asia-Pacific region.

3 | COMPONENT-RESOLVED DIAGNOSTICS FOR FOOD ALLERGY

Diagnosis of food allergy relies heavily on the clinical history of an IgE-mediated allergic reaction. Skin prick tests (SPT) and serum-specific IgE (spIgE) are common first-line diagnostic tests to evaluate food allergen sensitization. These tests can be useful as supporting evidence to confirm an allergy diagnosis or determine when a food may be suitable to reintroduce, but they have limitations as a standalone test. SPT and spIgE have different sensitivity and specificity profiles for different foods. Serum specific IgE to food allergen components is increasingly utilized in the clinical setting and has been shown to have a superior diagnostic performance for certain food sources, notably superior to SPT, particularly in equivocal cases. 323,24 Table 1 summarizes the diverse diagnostic performance of food allergen components with a focus on the Asia-Pacific region.

3.1 | Peanut allergy

Geographic variability in peanut allergy diagnostics underscores the need for region-specific strategies, with component-resolved diagnostics like Ara h 2 showing differing performance between Asia and the Western countries, such as those in North America, Europe, and Australasia. A recent systematic review and meta-analysis of the diagnostic tests used in food allergy provides the most thorough summary of the diagnostic accuracy of several tests, including SPT, splgE to whole food proteins, and CRD.³ The review included 149 studies, with meta-analysis performed when three or more studies

Key message

Component-resolved diagnostics (CRD) demonstrates significant geographical variations in allergen sensitization patterns between Asia-Pacific populations and Western populations, highlighting the critical need for region-specific diagnostic approaches. The review reveals that established diagnostic markers and their clinical utility differ substantially across regions, as evidenced by the varying sensitivity and specificity of common allergen components such as Ara h 2 for peanut allergy between Asian and Western populations. Additionally, unique sensitization patterns are observed in shellfish, fish, wheat and fruit allergies specific to the Asia-Pacific region. while aeroallergen profiles, particularly for pollens and house dust mites, show distinct regional characteristics influenced by local environmental factors. These findings underscore the importance of developing and validating region-specific CRD approaches rather than universally applying Western diagnostic standards, as this could improve the accuracy of allergy diagnosis and management strategies in the diverse Asia-Pacific region. Further research into locally relevant allergens and their components is essential for advancing targeted immunotherapy and patient care in this region.

were found for a given index test and food. Serum specific IgE to peanut components demonstrated high specificity for several components, including Ara h 2 (92%), Ara h 3 (93%), Ara h 6 (94%) and Ara h 8 (99%). However, the sensitivity was good in only Ara h 2 (82%) and Ara h 6 (87%) at cut-offs of 0.44 and 0.4kUA/L, respectively. All other components had sensitivity below 50%. Data on Ara h 8 and Ara h 9 splgE is heterogeneous and appears to be of limited clinical use. Meta-analyses for Ara h 2 splgE demonstrated maximum sensitivity (0.90) at 0.2kUA/L and maximum specificity (98%) at 1.15kUA/L.³ Most of the data analyzed in this systematic review come from Europe and North America, which limits its applicability in other populations.

There is geographic variability in the accuracy of CRD tests worldwide, including within the Asia-Pacific region. In Australia, Ara h 2 splgE testing, assessed in the HealthNuts study in a random sample of 200 infants (100 with OFC-confirmed peanut allergy and 100 with peanut tolerance), was integrated into a diagnostic algorithm. In this approach, Ara h 2 splgE testing was only performed for children with skin prick test (SPT) results in an intermediate range (3–8 mm). This algorithm demonstrated higher diagnostic accuracy than whole peanut splgE, with 60% sensitivity (95% CI, 50–70) at 98% specificity (95% CI, 93–100), and reduced the need for oral food challenges by nearly two-thirds when used in combination. In contrast, peanut SPT demonstrated the best diagnostic performance in Hong Kong children (3.7 mm threshold, sensitivity 93%, specificity 89%), while

TABLE 1 Key findings in food allergen sensitization and diagnostic patterns across the Asia-Pacific region.

Ref	(116)	(116)	(2)	(35)	(48)	(42)	(58)	(57)
Key Findings	95% PPVs for HK: 5.6 mm (SPT), 8.4 kUA/L (peanut splgE), 2.4 kUA/L (Ara h 2); good sensitivity with adjusted cut-offs.	95% PPV: 13mm (SPT), 34kUA/L (peanut splgE), 4.26kUA/L (Ara h 2); Ara h 2 most sensitive (90%).	Ara h 2 superior diagnostic tool compared to whole peanut splgE, reducing OFCs by two-thirds.	Pen m 1, Pen m 6, Pen m 13 and Pen m 14 are major shrimp allergens. Component test is superior compared to shrimp extract splgE and SPT	Japanese participants showed broader IgE binding, including grass carp, despite lower IgE levels. Parvalbumin is the main allergen in both groups, with higher enolase sensitization in Japan. Monosensitization to parvalbumin is common	Chinese patients show greater PV-splgE diversity than Austrian, Spanish, or Norwegian patients, independent of symptoms, age, or gender. Up to 41% of fish-allergic patients may tolerate one bony fish based on PV-splgE absence. Negative IgE to tuna PV predicts ≥90% likelihood of negative IgE to other beta-PVs, excluding salmon (71%), aiding tailored FC panels	ω5G splgE has better sensitivity than wheat splgE	ω5G splgE has better sensitivity than wheat splgE (83.3% vs. 50%)
Frequency of splgE to Allergen	SPT 3.7 mm threshold, sensitivity 93%, specificity 89%),	Ara h 2 0.35 kUA/L threshold, sensitivity 91%, specificity 87%	60% sensitivity, 98% specificity for Ara h 2	Hong Kong: Pen m 4, 6, 13 AUC 0.77-0.78; Thailand: Pen m 4 AUC 0.96, Pen m 1 AUC 0.89	- 60.0% (HK) and 66.7% (Japan) sensitized to 10kDa parvalbumin - 40.0% (Japan) sensitized to 130kDa collagen and 58 kDa enolase	- 74.7% sensitization rate to PV overall - 19% (total) and up to 38% (China) negative to cod PV - 25% negative to sole PV - 78% negative to ray PV	Wheat splgE 10.1 threshold sensitivity 61%, specificity 74%, 005G splgE 0.41 threshold sensitivity72%, specificity 79%	SPT accuracy 76.6%, wheat splgE(threshold 0.35) accuracy 90%, ω5G splgE (threshold 0.35) accuracy 76.7%
Allergens Tested	Peanut extract, Ara h 2; SPT peanut extract	Peanut extract, Ara h 2; SPT peanut extract	Ara h 2, Whole peanut	Pen m 1, Pen m 2, Pen m 3, Pen m 4, Pen m 6, Pen m 7, Pen m 8, Pen m 13, Pen m 14, SPT shellfish extract, splgE shrimp extract	Salmon and grass carp proteins, including parvalbumin, enolase, collagen, aldolase, and GAPDH	Parvalbumin (PVs) from various bony fish species	wheat extract, ω5G	SPT wheat, wheat extract, ω5G
Number of Participants	133	167	100 OFC-confirmed peanut allergy; 100 with peanut tolerance	85 (Hong Kong: 17 OFC-confirmed shrimp allergic; 32 probable shrimp allergy, 20 OFC-confirmed shrimp tolerant. Thailand: 16 physician-diagnosed shrimp allergy)	45 (30 from HK, 15 from Japan)+2 non-atopic controls	Not specified	311	30
Cohort	Peanut allergy	Peanut allergy	Peanut allergy	Shrimp allergy	Fish-allergic individuals	Fish-allergic individuals	Wheat allergy	Wheat allergy
Country	Hong Kong	Singapore	Australia	Hong Kong; Thailand	Hong Kong (HK) and Japan	China, Austria, Spain, Norway, Luxembourg	Japan	Thailand
Study Type	Retrospective	Retrospective study	Cohort study	Prospective study	Prospective study	Cross-sectional study	Retrospective	Cross-sectional Thailand study

Ara h2 performed best in Singapore children (0.35 kUA/L threshold, sensitivity 91%, specificity 87%), with both requiring higher thresholds than international standards to achieve a 95% PPV. These findings are based on OFCs conducted in all 300 children, highlighting the robust nature of the diagnostic comparisons. ¹¹⁶ Other geographical areas with a Western culture, such as Europe and North America, demonstrate similar sensitivity and specificity to Australia. Sensitivity and specificity are influenced by disease prevalence, which is lower for peanut allergy in Asia (0.27% (95% CI 0.12–0.42) compared to Australia (3.1% (95% CI 2.3–4.1)). ^{25,26}

Pollen food allergy syndrome (PFAS) causes oral tingling, itching or soreness of the mouth, ears, or throat when consuming raw plant foods.²⁷ It occurs due to homology between pollen allergens (such as profilins, lipid transfer proteins, and pathogenesis-related class 10 proteins) and food proteins. ²⁸ The related oral allergy syndrome (OAS) is a similar phenomenon, but PFAS could be considered a more severe presentation.²⁹ Peanuts have been described in PFAS worldwide, including in Australia, but are uncommon in Asia. 28,30 Diagnostic recommendations include component splgE tests such as Ara h 8 splgE to diagnose PFAS or Ara h 1, 3, and 6 to diagnose IgE-mediated allergy in the absence of a positive Ara h 2 splgE. 27 Given the low prevalence of PFAS in Asian countries and the poor diagnostic accuracy of these components, they are less relevant in diagnostic testing for this area. However, recent studies in this region suggest that in some countries, PFAS may be more prevalent, affecting as many as 10% of adolescents²⁹ Locally relevant pollen allergens such as Cyr j 2 or Art v 3, in conjunction with Bet v 1 and Bet v 2, may be diagnostically useful^{29,31} (Also see Table 2 and Pollen allergens below).

3.2 | Shrimp allergy

Research has shown geographic and phenotypic variability in shrimp allergy, particularly in the Asia-Pacific region. The first major allergen identified in crustacean shellfish was tropomyosin, and sensitization to tropomyosin is strongly linked to the incidence of shrimp anaphylaxis. 32,33 This muscle protein has been considered a good predictor of shrimp allergy, with positive and negative predictive values of 0.72 and 0.91, respectively.³⁴ Tropomyosin remains an important panallergen in the Asia-Pacific region, with sensitization rates around 60% in doctor-diagnosed shrimp allergic patients.³⁵ However, sensitization to Pen a 1 (tropomyosin) varies with geography, with rates ranging from 40% in challenge-proven shrimp allergic patients from China to 82.8%–98% in challenge-proven patients from Brazil and Spain. 34,36 A study that compared the sensitization patterns and diagnostic values of shrimp allergens in two distinct populations-subjects with challenge-proven or doctor-diagnosed shrimp allergy from Hong Kong (n=69) and Thailand (n=16), found leading shrimp allergens associated with clinical manifestations of shrimp allergy were sarcoplasmic calcium-binding protein (SCP), troponin C, fatty acid-binding protein, hemocyanin, and the newly identified high molecular weight allergen, glycogen phosphorylase. 37 These allergens had greater diagnostic accuracy for shrimp allergy compared to tropomyosin, based

on area under the curve (AUC) values of 0.77-0.96 compared to 0.70 for tropomyosin.³⁵ Hemocyanin, a heat-stable, high molecular weight allergen mainly found in the cephalothorax, was associated with anaphylaxis³⁸ and consistently identified as a clinically important allergen in Italian and Thai shrimp allergic subjects.^{39,40} The recent report indicated that tropomyosin did not appear to be a major allergen for shrimp allergy in Central Europe, particularly in patients with a house dust mite allergy.⁴¹ On the other hand, SCP was considered

to be more clinically important, as reported in multi-center studies in Asia and the United States.^{35,41} Emerging research suggests that

novel shrimp allergen components may have potential clinical utility

in diagnosing shrimp allergies and correlating with patients' clinical

presentations. Additional studies will be necessary to fully elucidate

the clinical implications of these emerging allergen markers and their

relationship to different shrimp allergy phenotypes.

3.3 | Fish allergy

Fish allergy diagnostics in the Asia-Pacific region differ from Western countries, with regional variations in the prevalence and relevance of specific allergens like parvalbumin (PV), collagen, and enolase. Parvalbumin has been known as the major fish allergen in bony fishes for more than 50 years and is included in routine diagnostics. While PV was the sole fish allergen (100% sensitization) in patients from China when tested against carp, mackerel, salmon, swordfish and tuna, up to one-third of patients from Austria, Denmark, Luxembourg, Norway, and Spain were IgE-negative to these PVs. 42 The varying crossreactivity among patients may stem from variations in IgE-binding epitopes across PV isoforms. 43 For instance, seven PV isoforms were identified in Indian mackerel,44 while Japanese scad exhibited four distinct allergenic PVs. 45 Enolase, aldolase and collagen are other important fish allergens beyond PV, alongside other less characterized allergens such as triosephosphate isomerase (sensitization 19%-34%), tropomyosin (6%-32%), pyruvate kinase, and glyceraldehyde-3phosphate dehydrogenase (GAPDH).46 Unlike the high sensitization rates to aldolase and enolase reported in Europe (50% and 62.9% respectively),⁴⁷ aldolase and enolase were less relevant fish allergens in Asia-Pacific regions. Sensitization to these allergens ranged from 15% in Japanese patients to 35% in Australian patients and could be as low as 4.3% in patients from Hong Kong. 46,48 Collagen, on the other hand, has been consistently reported as clinically important in the Asia-Pacific region. Apart from being a common sensitizer (21% in Australia, 30.4%-43.% in Hong Kong, 17.8%-50% in Japan), monosensitization to collagen was also reported in up to 38% patients. 48-51 These overall highlight the need to include collagen beyond parvalbumin in the diagnostic workup in the Asia-Pacific region.

3.4 | Wheat allergy

Wheat allergy, including wheat-dependent exercise-induced anaphylaxis (WDEIA), is best diagnosed using specific allergens like omega-5

TABLE 2 Frequency of splgE reactivity with pollen allergen components in patients with allergic diseases from the Asia-Pacific region.

Study type	Country	Cohort	Number of participants	Testing method
Retrospective	Peking (temperate) China	history of pollinosis with OAS; 68% FA; 10% drug allergy	402 (Mean 30.4 yr, range 8–84; 47% M)	ImmunoCAP,
Retrospective ^a	Beijing, (temperate) China	Allergy department outpatients with pollen allergy	547 Mean age: 28.4yr SD 14.3yr M 49.4%	ImmunoCAP
Cross-sectional ^a	Guangzhou, (subtropical) China	Group 1: CCD positive patients Group2: CCD negative patients	78 (34.6% <18 yr, 44.9% 18-60 yr, 20.5% >60 yr 72% M)	EUROBlotMaster
Cross-sectional ^a	Beijing, (temperate) China	birch pollen allergy with AR, +/- PFAS to apple	58 median 30 (17.8-38.2) yr; 53.4%	ImmunoCAP
Cross-sectional	Guangzhou, (subtropical) China	AD patient serum randomly taken from the serum bank (Jan 2020 to May 2020)	34 Mean age: 18.5 M: 47%	ImmunoCAP, ALEX
Observational ^a	Guangzhou, (subtropical) China	physician-diagnosed mild to moderate AR with/without asthma	258 patients, 88 controls (74.1% > 40 yr 60.3% M)	ImmunoCap
Cross-sectional	Guangzhou, (subtropical) China	Any allergic disease with history of contact and splgE reactivity to at least two pollen allergens	165 (69 < 18 yr; mean 7.21 ± 4.26 yr, 96 > 18 yr (mean 47.24 ± 15.53 yr) 67.2% M	ImmunoCAP screening; CRD by EuroImmune
Cross-sectional/ cohort	Tokyo, (temperate) Japan	General adolescent cohort checked for pollen allergy; 56.5% AR; 16% OAS; 11.7% PFAS (T-child Study)	506 13yr M: 49.2%	ISAC
Prospective birth cohort	Japan (Mostly temperate)	General population, School children	984 aged 5yrs. (2008 and 2010), and 729 aged 9yrs. (2012 and 2014) 49.8% M	ISAC, ImmunoCAP
Case-control	Machida, (subtropical) Japan	patients with birch pollen allergy-related OAS to apple or peach	30 OAS, 10 controls (median 36.5yr, range 18-79yr; 50% M)	ImmunoCAP
Retrospective	Seoul, (temperate) South Korea	birch pollen-sensitized, +/- OAS, or history of anaphylaxis to peanut.	81 Birch pollen-sensitized. 12 with peanut anaphylaxis (Mean 30.3 yr ±15.3 M/F: 50:50	ImmunoCAP, SPT
Cross-sectional	Seoul, (temperate) South Korea	A: 18 patients no OAS B: 13 patients with OAS after apple or peach	31 (Mean 8.61 ± 2.81 yr; 67.7% M)	ImmunoCAP, ISAC
Cross-sectional	Seoul, (subtropical) South Korea	allergy patients, plus 12 negative controls	50 (Mean 23 yr, 6–66 yr; 62% M)	ELISA ImmunoCAP, BAT
Cross-sectional	Seoul, (subtropical) Korea	Humulus japonicus (Cannabaceae) weed pollinosis symptoms, plus 22 healthy controls	22 Mean 43.5 yr 12–70 yr; 41% M	SPT or ImmunoCAP screening, ELISA, Immunoblot
Cross-sectional ^a	Queensland Sydney, Perth and Adelaide (temperate - subtropical), Australia	159 GP-allergic AR patients; 50 other allergy donors; 29 non-atopic controls	238 adults (Median 39 yr; IQR; 33.1% M)	ImmunoCAP, SA-ImmunoCAP
Retrospective ^a	Brisbane, (subtropical) Australia	grass pollen-allergic AR patients	48 adults Median 36.5 yr IQR 28.8-44.5 yr 29.7% M	ImmunoCAP ELISA
Cross-sectional ^a	Melbourne, (temperate) Australia	seasonal AR, with or without asthma	51 adults	ELISA splgE, splgE cross-reactivity, BAT

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; av, average; BAT, basophil activation test; CCD, cross-reactive carbohydrate components; CRD, component-resolved diagnostics; ELISA, enzyme-linked immunosorbent assay; FA, food allergy; GP, grass pollen; ISAC, Immuno-solid-phase Allergen Chip; LTP, lipid transfer proteins; PFAS, pollen food allergy syndrome; PR-10, pathogenesis-related class 10 proteins; SA, streptavidin; splgE, specific IgE; SPT, skin prick test; yr, years.

^aArticles reporting on pollen CRD in AR in Asia-Pacific were identified with the following search terms: Allergic rhinitis, Rhinitis, Pollen, Allergy, Allergen, CRD, Component-resolved diagnosis, Prevalence, Weed, Grass, Tree, Group 1 allergen, Asia-Pacific, China, Japan, Korea, Australia, Malaysia, Taiwan, and India in PubMed, Google Scholar, and Scopus.



Pollen source/Allergens tested	Frequency of spigE to allergen	Key findings	Ref.
Birch, mugwort, Bet v 1, Bet v 2, Art v 1,	In PFAS:	Art v 3 splgE levels might indicate food anaphylaxis in OAS	(31)
Art v 3, Pru p 1, Pru p 3	Art v 3: 79% Bet v 1: 85%	ALLY O Sprige revers might indicate rood unaphyddias in OA O	(01)
Grass, tree and weeds, Bet v 1, Bet v 2, Bet v 4, Amb a 1, Art v 1, Phl p 1, Cyn d 1, Phl p 5b, CCD	Cyn d 1: 34% Phl p 1: 7% Phl p 5b: 2% CCD: 11%	71.1% AR patients sensitized to grass pollen; Bermuda splgE highest (97%), CRD is useful for diagnostics	(95)
Bermuda grass Timothy grass Mugwort, recombinant Cyn d 1, Cyn d 12, Phl p 1, Phl p 12, Art v 4, and nArt v 1, CCD	rCyn d 1: 47.8% in CCD -ve vs. 14.5% in CCD+ve; rPhl p 1: 26.1% in CCD -ve vs. 7.3% in CCD+ve Art v 4: 26.1%	AR patients (esp children) had higher rCyn d 1 splgE; all Cyn d 12+ve patients had asthma; CRD splgE patterns varied by age	(117)
birch pollen allergen, bet v 1, Bet v 2, Bet v 4 and Bet v 6	Bet v 1:82.8%, Bet v 2: 29.3%, Bet v 6: 1.7%, Bet v 4: 0%	77.6% splgE to any component; $19%$ to two; level Bet v 1 splgE associated with PFAS	(118)
Cypress, cedar Ryegrass, ash, 125 allergens	Cup s 1: 14.7% Cry j 1: 14.7% Lol p 1: 11.8% Fra e 1: 8.8%	70.6% positive for >1, 52.9% for >2, 17.6% for >5, and 2.9% for >10 components, Der p1 (20.6%) was highest	(94)
Bermuda, Timothy	Cyn d 1: 53.4%, Phl p 1: 17.1%, Phl p 5: 8.6%, Phl p 4: 41.4% of BeGP; 100% of TGP positive	A higher BeGP-splgE (22.5% v TGP 13.6%); Cyn d 1 splgE may be important, but CCD may confound	(119)
Mugwort, Ragweed, goosefoot, walnut, birch, CCD, allergen molecules	Art v 1: 18.0%, Art v 2 and 3: 24.6% Amb a 1: 7.5% Bet v 2: 40%	Weed pollen splgE higher in adults; extracts strongly correlated with CCD; splgE with allergens not high (Amb a 1; 7.5%- Bet v 2: 40%)	(92)
Japanese cedar, Cypress, white birch, alder, Ragweed, timothy grass, 112 components	Cry j 1: 95.7% Cup a 1: 86.0% Bet v 1: 36.0%; Be tv 2: 10.5%; Bet v 4; 1.5% Aln g 1: 28.3% Amb a 1: 27.9% Phl p 1: 9.0%	72.7% sensitized to pollen; PFAS is common (10%) in adolescents in Japan; kiwi, pineapple and peach common for PFAS, most had poor knowledge about PFAS.	(29)
Japanese cedar Cypress, 112 allergens	Cry j 1: 32.8% at 5yr 57.8% at 9yr Cup a 1: 12.3% at 5yr 46.1% at 9yr	74.8% sensitized at 9 yrs.; Cry j 1 highest frequency overall; rates of AR and CRD splgE increased with age	(120)
birch pollen, appley, peach, PR-10, profilin, LTP	Bet v 1: 93.3% Bet v 2: 6.7% OAS; Mal d 1: 92.3%; Pru p 1 95.7%	CRD more sensitive and specific than extracts for the diagnosis of birch pollen-related OAS	(85)
Birch and oak pollen	Bet v 1: 82% Bet v 2: 19.7%. 4 with OAS also had Ara h 2 and Ara h 8 splgE	Fagales pollen may influence rates of OAS; Bet v 1, Ara h 2 and Ara h 8 splgE may indicate OAS	(121)
birch pollen, Bet v 1, Bet v 2, and Bet v 4	Bet v 1: A, 61% vs. B, 100% Bet v 2: A, 0% vs. B, 31% Bet v 4: both A and B: 0%	CRD sensitization profiles differed according to the presence of OAS	(91)
Mongolian Oak	Que m 1: 92% Que. a 1: 74% Bet v 1: 38%	Que m 1 and Bet v 1 BAT similar; Que. m 1 may be useful for the diagnosis of tree pollinosis	(99)
Japanese hop (Humulus japonicus)	Hum j 6: 86.4%	Hum j 6 identified as major weed allergen	(98)
Bahia grass, Bio-nPas n 1	Pas n 1: 92.4%	Bahia GP is an important pollen in subtropics; Pas n 1 IgE accounts for most of BaGP-splgE.	(122)
Johnson grass (Sorghum halepense)	Sor h 1: 97.5% Sor h 13: 43.8%	Sor h 1, Sor h 13 are important allergens; Sor h 2 and Sor h 23, but no group 5, allergen present	(123)
Bahia, Bermuda and ryegrass, nPas n 1, nCyn d 1, nLol p 1	Extract frequencies 90%–92%; Lol p 1 splgE > Pas n 1 or Cyn d 1	Sensitization to Ryegrass pollen and LoI p 1 higher in temperate $$	(124)

gliadin (ω 5G), with in-house extracts offering higher diagnostic accuracy compared to commercial wheat extracts, especially in the Asia-Pacific region. Wheat protein can be classified into either water/salt-soluble albumins and globulins or water/salt-insoluble gliadins and glutenins. ⁵² Omega-5 gliadin was identified as the major allergen for IgE-mediated wheat allergy. ^{53,54} Recently, a study from Thailand showed that alpha/beta/gamma gliadins were important allergens in children with wheat anaphylaxis. ^{55,56} The commercial wheat extract typically contains a mixture of various wheat proteins, which may dilute the allergenic components, including gliadins, leading to a lower diagnostic accuracy. In contrast, the in-house extract is customized to focus more on gliadins and glutenins, which are the key allergens, improving the sensitivity and diagnostic accuracy of the test. ⁵⁷ The accuracy for wheat allergy diagnosis by the commercial extract was 76.6% compared to 86.7% using the in-house extract. ⁵⁷

Levels of ω 5G-splgE potentially have better diagnostic capacity than wheat splgE, with AUC being slightly greater for ω 5G (78.5%) compared to wheat splgE (73%); sensitivity at the optimal cut-point was also higher for ω 5G (72%) compared to wheat splgE (61%). ^{58,59}

WDEIA is a specific clinical phenotype of food allergies. Omega-5 gliadin, gamma gliadin, and high molecular weight glutenin were previously reported as major allergens in WDEIA patients. 60,61 These allergens have been highlighted in several studies conducted in the Asia-Pacific region. For instance, in Japan, $\omega 5G$ is recognized as a critical allergen in WDEIA, with a cut-off value of 0.89 kUA/L for $\omega 5G$, the sensitivity for diagnosing WDEIA is 78%, while the specificity is 96%. 62 In Thailand, the in-house gliadin/glutenin extract generally has a better diagnostic yield for WDEIA diagnosis than the commercial skin SPT extract. 63 A new subtype of WDEIA with reactions to hydrolyzed wheat protein (HWP-WDEIA) has been reported in Japan. Compared to conventional WDEIA, patients with HWP-WDEIA are more sensitized to gluten but not $\omega 5G$ -splge. 64

3.5 | Fruit allergies

Fruit allergies in the Asia-Pacific region exhibit diverse patterns. Largely based on self-report and/or physician diagnosis but without OFCs, the prevalence of fruit allergy ranged from 0.1 to 4.3% in 2009, 65 with a recent review showing it now varies from 0.029% to 8%, influenced by settings, populations, and case definitions. 66 The Rosaceae family (peach, apple, apricot, pear, raspberry, strawberry) and non-Rosaceae fruits, such as kiwifruit, are common causative fruits in Europe. 67,68 Since the types of tropical fruits vary depending on the region and climate zone, a diverse pattern of Rosaceae and non-Rosaceae allergies is observed in the Asia-Pacific region—Rosaceae fruit allergies are common in Japan, 69 mango allergies in East Asia (China and Taiwan), 70-73 and banana and kiwi allergies in Southeast Asia (Thailand), 74,75 South Asia (India), 76 and West Asia (Iran, Israel, Turkey). 77-80 In contrast, a recent US survey (2015–2016) found fruit allergies to be rare, likely due to the exclusion of cases with OAS. 9,81

Fruit allergies can range from localized symptoms to anaphylaxis, often due to primary sensitization to pollen allergens, with

cross-reactive IgE binding to plant food, known as Pollen Food Allergy Syndrome (PFAS). Lipid Transfer Protein (LTP) syndrome, a condition involving allergic reactions from at least two unrelated LTP food allergens, is now recognized in countries like China, Japan, South Africa, and Australia. Latex-fruit syndrome (LFS) is another entity that involves allergic reactions to both latex and various fruits, such as avocado, banana, kiwifruit, and chestnut. Class 1 chitinases (Hev b 6) play a significant role in LFS and exhibit high sequence homology with chitinases in related fruits.

Compared to Western countries, there is a paucity of molecular sensitization data on fruit allergies in the Asia-Pacific region. So far, few studies on fruit allergy CRD have been conducted. In China, the major allergenic proteins in mango are Man i 1 (class IV chitinase), Man i 2 (Bet v 1-related protein), and Man i 4 (profilin).⁸⁴ In a large Japanese cohort, Bet v 1 homologs and profilin were sensitized in most cases, indicating the PFAS mechanism. Gibberellin-regulated protein (GRP), represented by peach Pru p 7, is common in non-PFAS patients, while LTP is found in a minority of patients.⁶⁹ The finding is similar to another Japanese group.⁸⁵

Further molecular epidemiology studies are needed for diagnostic utility and interpretation of CRD results in the Asia-Pacific region, as allergen components are specific to certain fruit species, some of which are unique to this region.

4 | COMPONENT-RESOLVED DIAGNOSTICS FOR AEROALLERGENS

Asthma and AR affect millions of children globally, but many asthma and AR patients are not investigated for underlying aeroallergen sensitizations. Timely diagnosis of aeroallergen sensitizations in children with airway allergies can predict asthma development, medication response, and future exacerbation, and is important in guiding personalized treatment plans and the initiation of allergen-specific immunotherapy.^{86,87}

4.1 | Pollens

Pollen is considered a primary cause of allergic rhinitis (AR) in some regions of Asia-Pacific. For instance, the frequency of sensitization to Japanese cedar (*Cryptomeria japonica*) pollen is as high as 68% of the population tested, and this pollen causes AR in as many as 40% of people in Japan. ⁸⁸ However, in tropical regions, pollen allergy may be less important; in Malaysia, Taiwan and Thailand, the sensitization of AR patients to grass pollen ranges from 6.5 to 20.5%, 2.5 to 10%, and 16 to 21%, respectively, depending on species tested (Bermuda; *Cynodon dactylon*, Johnson; *Sorghum halepense*, or Bahia; *Paspalum notatum*). ⁸⁹ House dust mite showed the highest sensitization rates in southern China, with a subtropical climate, whereas weed pollens of mugwort, ragweed, and dandelion showed the highest frequencies in northwestern China, where the climate is temperate. ⁹⁰

Climate, topography, and other biogeographical conditions influence plant distribution, species diversity, pollen abundance, and therefore, pollen allergenicity profiles. Diagnosis has largely relied on SPT with extracts of pollen, particularly those relevant to temperature climate zones of Europe. This may underrepresent true sensitization, and more importantly, fail to reveal the specific pollen sources associated with a person's symptoms in the Asia-Pacific region. Patients with seasonal AR or allergic asthma are often exposed to multiple different pollens, which may contain common allergen families; for example, beta-expansins (Pas n 1, Cyn d 1) and polygalacturonase (Pas n 13) in grass pollen, profilin (e.g., Bet v 2) and pectate lyase (e.g., Cry j 1) in tree pollen, and defensins (Art v 1, Amb a 4) in weed pollen, leading to apparent poly-sensitization by SPT or splgE with multiple pollen extracts. The presence of panallergens in multiple pollen sources, such as profilin (e.g., Phl p 12), polcalcin (e.g., Phl p 7 or Bet v 4), LTP (e.g., Art v 3), and PR-10 (e.g., Bet v 1), may not only confound diagnosis of pollinosis but, in some cases, may be associated with OAS and PFAS in this region, including China, 31 Japan, ²⁹ and Korea ⁹¹ (Table 2). A number of pollen allergens, like natural Cyn d 1, Phl p 4, and Cry j 2, contain cross-reactive carbohydrate determinants (CCDs),⁴ potentially confounding diagnosis.⁹² Studies from the Philippines, where grass pollen allergy is low, have shown for unselected allergy patients that grass pollen splgE detected using timothy or Bermuda grass pollen allergens, including natural Cyn d 1 and Phl p 4, can be blocked with other components containing CDDs. 93 Use of recombinant allergens, rPas n 1 and rCyn d 1 lacking CCDs, or comparison of allergen component with CCDs may therefore improve specific diagnosis of pollen allergy. 94-96

Table 2 collates data from studies within this geographic region that report on spigE to allergen components of tree, weed and grass pollens in general populations, AR patients with or without asthma, OAS, or PFAS.

Considering migration, patients who relocate to a new region may experience changes in pollen exposure and symptoms if pollens to which they were sensitized in their previous residence do not fully overlap with the allergens present in their new environment. 97 There are continuing processes of characterization of locally relevant pollen allergens including Hum j 6 of Japanese hop, 98 Que. m 1 of Mongolian oak, 99 Uro m 1 of Para grass, 100 Zoy m 1 of Manila grass, ¹⁰¹ and a number of Artemisia allergens related to Mugwort pollen from northern China that have been listed by the International Union of Immunological Society Allergen Committee. 102 It will be important to see further studies on sensitization rates in relevant areas and their clinical importance for particular patient groups across the Asia-Pacific region.

4.2 House dust mite allergy

Dermatophagoides pteronyssinus (Der p) and D. farinae (Der f) are the most common house dust mites (HDM) worldwide. The allergenic reactivity of HDM has been well characterized to be dominated by the Group 1 (Der p 1 and Der f 1) and Group 2 (Der p 2

and Der f 2) allergen components, while Der p 23, a putative chitinbinding protein, is a newly recognized major allergen in HDM that has been found associated with severe asthma and allergic rhinitis symptoms. 103-105 Sensitization to Blomia tropicalis (Blo t) was prevalent in Southeast Asia, particularly Singapore and Malaysia, even more so than to Der p and Der f. 106,107 Comparison of studies conducted in the West and the East often points to similar sensitization rates and patterns to these allergens, with IgE binding to these allergens well exceeding 50% in HDM-sensitized cohorts. For instance, a recent study in Japan indicated 94.2% and 97.5% sensitization to Der p 1 and Der p 2, respectively, 108 compared to 73% and 80% in a multinational study in Canada, Europe, South Africa, and The States and 74% to >90% in Southern China. 109,110 The sensitization rate to Der p 23 was 64% in the West, 54.6% in Southern China and 71.7% in Japan. Yet, a comparison of the sensitization profile of cockroach-sensitized individuals showed remarkably lower sensitization to Der p 1 (35%), Der p 2 (48%), Der p 10 (15%) and Der p 23 (31%) in Austria than those from Hong Kong (97%, 88%, 52%, and 79% respectively). 111 In this context, HDM sensitization highly correlates with shellfish sensitization in warm, humid climates and urban environments where HDM are ubiquitous. 112 A prospective study also indicated that HDM sensitization at 18 months was associated with increased odds of shellfish sensitization at 8 years. 113 Der p 10, tropomyosin, has been initially recognized as the allergen responsible for cross-reactivity between HDM and shellfish due to the high sequence and structural homology. Despite its low prevalence among HDM-sensitized patients between 5% and 18%, sensitization to Der p 10 is strongly associated with a history of anaphylaxis to shrimp and shellfish. 114 Der p 20, arginine kinase, as well as hemocyanin and paramyosin, are other allergens beyond tropomyosin reported to be involved in the shellfish-HDM interrelationship. 115 Yet, whether shellfish allergy is a secondary phenomenon that follows HDM sensitization or a true primary allergy remains an open question to be answered.

CONCLUSION

Component-resolved diagnostics (CRD) are becoming a crucial tool for allergists in research and clinical practice. This review describes the geographical variances in CRD for food and aeroallergens in the Asia-Pacific region and prompts the need to adopt region-specific and tailored strategies in precision diagnosis. While peanut components, such as Ara h 2, significantly improve diagnostic accuracy in Western countries where PFAS is prevalent, their utility in Asia may be limited. Tropomyosin is a major shellfish allergen, especially in the Asia-Pacific region, but it may not be the sole or primary allergen in all populations. Other emerging allergens, such as SCP and troponin C, may be better indicators of clinical shrimp allergy than tropomyosin in some cases.

Pollen is a common cause of allergic rhinitis in parts of Asia-Pacific, but the specific pollen allergens differ by region due to factors like climate and geography. Reliance on pollen extracts from temperate regions may not capture all relevant sensitivities. The presence of cross-reactive allergen components like profilins and polcalcins in multiple pollen sources can confound the diagnosis of pollinosis and lead to apparent poly-sensitization. Besides, HDM is a major aeroallergen globally, with Der p 1, Der p 2, Der p 23, and Blo t 5 being the dominant allergens in the Asia-Pacific region.

CRD evidently helps in identifying and understanding sensitization to allergens that are unique to particular clinically important allergen sources, which may be more or less prevalent or show biogeographically distinct prognostic utility in the Asia-Pacific region. This information is important for developing region-specific allergy management guidelines and public health policies. We must move forward by adapting CRD panels to fit the regional context and ensuring improved access to and adoption of CRD testing. Additionally, we must prioritize region-specific research and data sharing to expand our understanding of sensitization patterns' epidemiology in diverse Asian populations and ensure the availability for diagnostic use of regionally relevant, well-defined allergen components of food, and aeroallergen sources.

AUTHOR CONTRIBUTIONS

Carmen Riggioni: Conceptualization; writing – original draft; writing – review and editing; supervision. Agnes Sze-Yin Leung: Conceptualization; writing – original draft; writing – review and editing; supervision. Christine Yee-Yan Wai: Writing – original draft; writing – review and editing. Janet M. Davies: Writing – original draft; writing – review and editing. Mongkhon Sompornrattanaphan: Writing – original draft; writing – review and editing. Punchama Pacharn: Writing – review and editing; writing – original draft. Sajjad Chamani: Writing – review and editing; writing – original draft. Tim Brettig: Writing – original draft; writing – review and editing. Rachel L. Peters: Writing – original draft; writing – review and editing; conceptualization; supervision.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/pai. 70054.

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How to cite this article: Riggioni C, Leung A-Y, Wai C-Y, et al. Exploring geographical variances in component-resolved diagnosis within the Asia-Pacific region. *Pediatr Allergy Immunol.* 2025;36:e70054. doi:10.1111/pai.70054