

# ALLERGIC SENSITISATION IN SOUTH AFRICA: ALLERGEN-SPECIFIC IGE-COMPONENT TESTING (ISAC)

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## ABSTRACT

**Background:** Allergic sensitisation patterns differ globally; therefore it is important to understand local South African sensitisation patterns to inhalant and food allergen components to enable clinicians to diagnose and manage South African patients appropriately.

**Methods:** A retrospective study was conducted reviewing component allergen testing data from a private laboratory provider in South Africa over a two-year period. Data generated from all Immuno Solid-phase Allergen Chip (ISAC) tests referred from all regions in South Africa were collected and analysed according to the allergen-component positivity rate.

**Results:** A total of 813 consecutive patients were tested for allergen-component sensitisation by ISAC testing. Data were assessed to determine the most prevalent sensitisation patterns for inhalant, food and cross-reactive allergen components. The most frequent inhalant allergen components were Bermuda grass (Cyn d 1) and Timothy grass (Phl p 1), followed by cat uteroglobin (Fel d 1) and house-dust mite (HDM) (Der f 1). Peanut (Ara h 2), shrimp (Pen m 2) and egg white (Gal d 1) were the most prevalent food-component allergens. The most common pollen–food cross-reactive allergen components were cross-reactive carbohydrate determinant (CCD), profilin and thaumatin-like protein (pathogenesis-related protein (PR-5)).

**Conclusions:** Grass pollen components were identified as the most common inhalant allergen sensitiser. The most common pollen–food cross-reactive component sensitisation was to CCD, which is in keeping with the high level of grass pollen sensitisation. HDM-component sensitisation was lower than expected when correlated with previous studies using whole allergen specific IgE sensitisation data. This study contributes to understanding allergen sensitisation patterns in South Africa by adding component sensitisation data to the current diagnostic knowledge pool; and it raises awareness of the extent of allergen-component cross-reactivity in South Africa.

**Keywords:** allergic sensitisation, allergen-specific IgE-component testing, sensitisation patterns, inhalant, food allergen component

## BACKGROUND

The era of molecular allergy diagnostics was introduced in 1988 with the sequencing of Birch pollen antigen Bet v 1 deoxyribonucleic acid (DNA). Sequencing technology allowed for many recombinant or purified allergen components to be identified and measured, which was first introduced as singleplex assays and as multiplex assays in 2001. The Immuno Solid-phase Allergen Chip (ISAC) has subsequently become a benchmark in the world of multiplex allergen-component diagnostics and has been in use in South Africa since 2009.

Allergen components used in the manufacture of allergy tests may be obtained from either natural or recombinant sources. Natural (n) sources of allergen molecules are more variable and may contain multiple molecular variants (isoforms) that bind

IgE with varying strength. Purified natural allergens could also generate false positive results due to the presence of N-glycan sugar side chains or cross-reactive carbohydrate determinants (CCD). One of the main advantages of the recombinant production of allergens is that they could be produced without CCD.<sup>1</sup> Therefore, to improve standardisation and reduce CCD cross-reactivity, recombinant (r) allergen molecules are used predominantly.<sup>2</sup>

Allergens are assigned names based upon their taxonomic nomenclature: the first three letters designate the genus, followed by the first letter of the species and an Arabic numeral denoting the order of identification, for example: Peach, Pru p 3 (*Prunus persica*).<sup>3</sup>

**TABLE I: THE MOST COMMON INHALANT ALLERGEN-COMPONENT SENSITISATION IDENTIFIED FROM ISAC DATA**

ABBREVIATION	IgE-SPECIFIC ALLERGEN COMPONENT	NUMBER OF POSITIVE SPECIMENS ( <i>n</i> = 813)	PERCENTAGE (%)
Cyn d 1	Bermuda Grass, Group 1 (Contains <b>CCD</b> )	330	40.60
Phl p 1	Timothy Grass, Group 2 (Contains <b>CCD</b> )	281	34.60
Phl p 4	Timothy Grass, Berberine Bridge enzyme (Contains <b>CCD</b> )	219	26.90
Fel d 1	Cat, Uteroglobin	153	18.80
Pla a 2	Plane tree, Polygalacturonase (Contains <b>CCD</b> )	137	16.90
Der f 1	D farinae, Cysteine protease	132	16.20
Der p 2	D pteronyssinus, NPC2 family	131	16.10
Der p 1	D pteronyssinus, Cysteine protease	130	16.00
Der f 2	D farinae, NPC2 family	124	15.03
Alt a 1	Alternaria, Acidic glycoprotein	123	15.10

Testing IgE antibodies to allergen components has improved allergy diagnosis and patient management by enabling clinicians to

- predict allergen cross-reactivity;
- predict the severity of reactions;
- assist in dietary avoidance advice;
- reduce food challenges; and
- select patients for allergen immunotherapy.

Sensitisation data used to interpret ISAC results have originated mainly from European studies and, despite ISAC testing being available for more than a decade in South Africa, there is still a paucity of local sensitisation data. This retrospective study aims to contribute to understanding allergen-component sensitisation patterns in South Africa. Local clinicians can use these data to improve patient management or to choose cost-effective singleplex component assays in selected patient groups.

## METHODS

Retrospective data on allergen-specific IgE-component testing (ie ISAC) were collected anonymously from AMPATH patient databases and analysed. The tests in question were performed from 1 January 2016 to 31 December 2017 at AMPATH, a national private pathology provider in South Africa. The ISAC assay was reformulated to include other allergen components in 2018; therefore, more recent data could not be included in this analysis. All patients, both adults and children, tested during the specified time frame were included in this study. Allergen-specific IgE-component testing was reported as a value from 0–100 ISU/L (International Standard Unit per litre). Allergen sensitisation was defined as the presence of allergen-specific IgE > 0.3 ISU. Levels of allergen-component-specific IgE of > 0.3–1.0 ISU was considered to be low positive, 1.0–15.0 ISU as moderately high positive and > 15.0 ISU as very high positive, in accordance with the manufacturer's instructions.

The research was conducted according to the Declaration of Helsinki. Ethics approval for this study was obtained from the University of Pretoria Health Research Ethics Committee, approval number 110/2019.

## RESULTS

A total of 813 consecutive patients were tested for allergen-component sensitisation by ISAC testing. Data were assessed to determine the most prevalent sensitisation patterns for inhalant, food and cross-reactive allergen components.

## DISCUSSION

Sensitisation data for the ISAC inhalant IgE component revealed that grass pollen sensitisation (Bermuda and Timothy grass) was the most common sensitiser overall, followed by cat (rFel d 1) uteroglobin, Plane tree pollen (nPla a 2) – contains CCD, HDM (D farinae (Der f 1, Der f 2)) and D pteronyssinus (Der p 1, Der p 2) and Alternaria (rAlt a 1). It was surprising to note that HDM sensitisation was lower than expected, as previous South African sensitisation data on ImmunoCap IgE as well as skin-prick testing (SPT) indicated HDM to be the most common sensitiser, followed by grass pollen.<sup>4</sup> This may be attributed to the geographic distribution of patients, as HDM sensitisation is more prevalent in coastal areas; or it could be attributed to patient selection bias, because ISAC testing is frequently requested on patients with food allergies.

The most common food-component IgE-sensitisation data revealed peanut (rAra h 2, nAra h 6) as the most common sensitiser overall, followed by shrimp (nPen m 2) and egg white, ovomucoid (nGal d 1). nPen m 2 can cause cross-reactions to crustaceans (eg crab, lobster) and insects (eg cockroach). Please note that shrimp component sensitisation may be influenced by cross-reactivity to HDM allergens.

Walnut (nJug r 2, storage protein) was the most prevalent food cross-reactive component sensitiser, followed by CCD (MUXF3), latex (Profilin, rHev b 8), kiwi (nAct d 2, Thaumatin-like protein), peach (rPru p 3, LTP) and walnut (nJug r 3, LTP). Please note that the Walnut component nJug r 2 is rich in CCD groups, which may indicate CCD cross-reactivity and not necessarily storage protein allergy. It is notable that nJug r 2 was removed from the latest version of the ISAC microarray test due to the high level of CCD cross-reactivity.

It is interesting that Thaumatin-like protein sensitisation is more common than LTP and Proteinase-10 (PR-10) sensitisation in the population in this study. This has an important impact on recommendations for individual ImmunoCap cross-reactive IgE-component testing for food–pollen syndrome, because Thaumatin-like protein is not available as a single-plex allergen component test.

Cross-reactive molecules complicate allergy diagnosis substantially, because there may be uncertainty as to which allergen is the primary sensitiser, or whether the test result

**TABLE II: THE MOST COMMON FOOD ALLERGEN-COMPONENT SENSITISATION IDENTIFIED FROM ISAC DATA**

IgE-SPECIFIC ALLERGEN COMPONENT	ABBREVIATION	NUMBER OF POSITIVE SPECIMENS (n = 813)	PERCENTAGE (%)
<b>Peanut</b>	Ara h 2 (Storage protein)	58	7.10
	Ara h 6 (Storage protein)	53	6.50
	Ara h 1 (Storage protein)	47	5.80
	Ara h 9 (LTP)	35	4.30
	Ara h 3 (Storage protein)	29	3.60
	Ara h 8 (PR-10)	11	1.40
<b>Shrimp</b>	Pen m 2 (Arginine kinase)	53	6.50
	Pen m 1 (Tropomyosin)	32	3.90
	Pen m 4 (Sacropasmic Ca binding protein)	13	1.60
<b>Egg white</b>	Gal d 1 (Ovomucoid)	42	5.20
	Gal d 2 (Ovalbumin)	33	4.10
	Gal d 3 (Conalbumin)	32	3.90
	Gal d 5 (Serum albumin)	20	2.50
<b>Cow's milk</b>	Bos d 6 (Serum albumin)	25	3.10
	Bos d 4 (Alpha-lactalbumin)	21	2.60
	Bos d 8 (Casein)	18	2.20
	Bos d 5 (Beta-lactoglobulin)	15	1.80
	Bos d lactoferrin	6	0.07
<b>Wheat</b>	Tri a aA_T1 (Alpha-amylase)	23	2.80
	Tri a 9 (Omega-5 Gliadin)	12	1.50
	Tri a 14 (LTP)	11	1.40

is positive as a result of a cross-reactive reaction. For this reason, an understanding of cross-reactive allergens is vital to helping ultimately to make the correct diagnosis, and then to advise the patient. A short review of the most important cross-reactive allergen components identified in the South African population studied, and their impact on clinical decision-making, is discussed in more detail below.

### STORAGE PROTEINS

Storage proteins are produced in seeds to supply energy, serve as a nutrient reserve to the developing seedlings and are present in all seeds. Seeds have been classified into cereal grains (eg wheat, rye, rice, corn and oats), legumes (eg peanuts, beans, lentils and chickpeas), tree nuts (eg walnut, hazelnut and almond) and others (eg buckwheat, sesame and mustard). Storage proteins occur in all of these groups of plant food.

Seeds are an important plant-food source in South Africa. The protein content in seeds is relatively high per dry weight (10% in the case of cereals, and 40% in legumes). Of this protein content, a large proportion is storage protein, which accounts for the high allergenicity of seeds.

Seeds need to survive in extreme environmental conditions and, as a result, heating or other food-processing does not affect the stability of storage proteins. Seeds are only partially digested in the stomach due to their increased stability, which leads to the availability of allergenic molecules in the gastrointestinal circulation. These characteristics contribute to their allergenicity.<sup>5</sup> Systemic reaction and anaphylaxis are a distinct possibility in an individual sensitised to storage proteins.

The majority of storage proteins belong to three families: 2S

albumins, 7S globulin and 11S globulins. Extensive cross-reactivity within the three families exists: for example, peanut (Ara h 2, 2S albumin) and almond (2S albumin). However, the clinical relevance of serological cross-reactivity among various legumes, nuts and seeds can be established only after a thorough history and food-challenge testing, if indicated.<sup>6</sup>

Component-resolved diagnostics may help to distinguish primary and pollen-associated sensitivity to legumes, nuts and seeds. Storage proteins have numerous isoforms and restricted cross-reactivity due to variable sequence homology; therefore, these proteins are not suitable as a marker of cross-reactivity in their entire protein family.

### Clinical application

If storage protein A and storage protein B (of the same protein family) have similar IgE concentrations, it is difficult to distinguish between dual sensitisation or a cross-reaction with an unknown primary source of sensitisation. If storage protein A's IgE concentration is higher than that of storage protein B (the same protein family), A is probably the primary sensitiser, but a provocation test and/or a clinical history would be necessary in order to establish whether the protein B cross-reaction is clinically relevant.<sup>7</sup>

### CROSS-REACTIVE CARBOHYDRATE DETERMINANTS (CCD)

In the process of glycoprotein biosynthesis, carbohydrate chains are progressively synthesised and covalently bound to various amino acids of a glycoprotein. Plants and invertebrates contain fucosylated and/or xylosylated N-glycans, which are not present in human beings; this explains the pronounced immunogenicity in human beings.<sup>8</sup> The multivalent occurrence of carbohydrate determinants in a protein partly determines allergenicity.

**TABLE III: THE MOST COMMON POLLEN–FOOD CROSS-REACTIVE ALLERGEN-COMPONENT SENSITISATION IDENTIFIED FROM ISAC DATA**

IgE-SPECIFIC ALLERGEN COMPONENT	ABBREVIATION	NUMBER OF POSITIVE SPECIMENS (n = 813)	PERCENTAGE (%)
<b>Storage protein/CCD (removed from latest ISAC assay due to high level of CCD cross-reactivity)</b>	Jug r 2 (Walnut) (Contains <b>CCD</b> )	173	21.30
<b>CCD</b>	CCD MUXF3	167	20.50
<b>Profilin</b>	Hev b 8 (Latex)	77	9.50
	Mer a 1 (Annual mercury)	72	8.90
	Bet v 2 (Birch)	70	8.60
	Phl p 7 (Timothy grass)	54	6.60
<b>Thaumatin-like protein (PR-5)</b>	Act d 2 (Kiwi)	61	7.50
<b>Lipid transfer protein (LTP)</b>	Pru p 3 (Peach)	42	5.20
	Jug r 3 (Walnut)	35	4.30
	Ara h 9 (Peanut)	35	4.30
<b>PR-10</b>	Mal d 1 (Apple)	20	2.50
	Bet v 1 (Birch)	14	1.70
	Pru p 1 (Peach)	11	1.40

Patients sensitised to CCD rarely respond clinically to CCD epitopes, as IgE-mediated effector-cell activation is dependent on cross-linking adjacent membrane-bound IgE molecules. But this occurs very rarely during binding with non-protein epitopes.

As seen from our data, 20–21% of South Africans tested in this study are sensitised to CCD. Grass pollen is a potent inducer of IgE antibodies to CCD groups, therefore it is postulated that the high level of IgE sensitisation to CCD in the South African population may be attributable to the high level of grass pollen sensitisation.

Of the 112 allergens included in the ISAC, six are glycosylated (possessing CCD side chains that could bind IgE). These components include walnut (nJug r 2), Bermuda grass (nCyn d 1), Timothy grass (nPhl p 4), Japanese cedar (nCry j 1), Arizona cypress (nCup a 1) and Plane tree pollen (nPla a 2). For this reason, a positive result should be interpreted in the context of IgE reactivity to the CCD marker MUXF3, because the IgE to these six components cannot differentiate between primary sensitisation to the protein or to the carbohydrate side chain (CCD).<sup>9</sup>

#### *Clinical application*

False positive allergen-specific IgE results to various food allergens could be as a consequence of cross-reactive anti-CCD IgE antibodies, as seen in the disproportionately high levels of IgE sensitisation to wheat, peanut and soya reported previously in South Africa. Owing to the low probability of significant clinical symptoms associated with CCD sensitisation, a patient sensitised to CCD alone could possibly avoid the unnecessary dietary exclusion of wheat, peanut and soya.<sup>4</sup>

#### PROFILINS

Profilins and polcalcins are classified as panallergens because of their ubiquitous distribution in various plant species and their high level of cross-reactivity. Profilins are actin-binding proteins and are present in various plant-derived foods, pollen and latex. Polcalcins are present in pollen and regulate intracellular calcium levels.

Panallergens are responsible for widespread cross-reactions between botanically unrelated plant species – for example, pollen, plant foods (ie melon, banana, citrus fruit, tropical fruits, cucumbers or various vegetables) and latex. Profilins are found in all eukaryotic cells and are involved in the control of multiple molecular processes within intracellular networks, which explains their high serological cross-reactivity.<sup>1</sup>

Profilin sensitisation of approximately 10% was detected in our data. Latex (rHev b 8), birch (rBet v 2) and annual mercury (weed) (rMer a 1) profilin represented the most prevalent profilin sensitisation in our South African dataset. South African sensitisation correlates more closely with German profilin sensitisation (10–15%), in contrast to Italian data, which demonstrated weed profilin sensitisation of approximately 30%.<sup>10</sup>

Profilins are heat-labile and unstable in the presence of digestive enzymes; therefore, it is suggested that pollens are the primary sensitisers of profilin allergies and not profilin-containing foods. Grass pollens are the most likely source of profilin sensitisation in South Africa. Sensitisation to birch (Bet v 2) and grass pollen (Phl p 7) profilins explains the cross-sensitisation to hazelnut and Rosaceae family fruits (strawberry Fra a 4, apple Mal d 4, cherry Pru av 4, almond Pru du 4, peach Pru p 4 or pear Pyr p 4). Profilin sensitisation is also responsible for the cross-sensitisation between birch and mugwort pollen and reactions to celery or carrot. Although profilins are highly cross-reactive in vitro, the clinical impact of profilin sensitisation is not always that relevant. Allergic reactions are usually mild and limited to tingling, itching or swelling of the oral mucosa and upper gastrointestinal tract and only in rare cases may more severe allergic reactions be triggered.

Local sensitisation to another panallergen's polcalcins could be demonstrated by birch (Bet v 4) and Timothy grass pollen (Phl p 7) component testing.<sup>10</sup>

#### *Clinical application*

Patients sensitised only to Hev b 8 (latex), the latex profilin, and to no other latex component would most likely be able to

tolerate latex.

Patients may test positive on allergen-specific IgE to wheat, peanut and soya due to profilin sensitisation. As symptoms upon ingestion may be either absent or mild, it is important to identify profilin as the source of sensitisation to avoid unnecessary dietary elimination. Profilins are heat-labile and degrade after processing; therefore, dietary advice could include the use of cooked or processed foods, which may be tolerated.

#### LIPID TRANSFER PROTEINS

Non-specific LTPs are involved in lipophilic binding and transport in plants, and also form part of the plant's defences. The four strong disulphide bonds in the LTP protein structure compact and stabilise the structure, contributing to a high thermal and proteolytic stability.<sup>11</sup> The outer surface (skin) of fruits contains especially high concentrations of LTPs. LTPs also accumulate in the seeds of fruit.

Clinical reactions towards LTPs may range from oropharyngeal allergic symptoms to anaphylaxis, and may be due to the consumption of foods but also to airway exposure or skin contact.<sup>11</sup> Primary sensitisation could occur to food LTPs or pollen LTPs, where one allergen source could be the primary sensitiser with cross-reactivity to homologous LTPs.

Peach (Pru p 3) LTP is the most common LTP sensitiser demonstrated in our South African data. It has also been described as such in southern Europe and the Mediterranean area.<sup>1</sup> Plane tree pollen may also be an important source of LTP sensitisation in South Africa, it also being well described in Mediterranean countries.

LTPs are expressed in foods (fruits, vegetables and seeds), in pollen (tree, grass and weed pollen) and in latex. There is a high level of IgE cross-reactivity between different sources of LTPs. Stone fruits are highly cross-reactive: for example, peach (Pru p 3), plum (Pru d 3), cherry (Pru av 3) and apricot (Pru ar 3). Mono-sensitisation possibly results in stronger clinical reactions. Patients sensitised at an earlier age to LTP are more likely to be primarily sensitised to peach LTP (Pru p 3).<sup>12</sup>

Peach LTP (Pru p 3) is commonly used as a marker for LTP sensitisation, although LTP sensitisation may not always be clinically relevant. However, in the presence of other contributing factors, such as physical activity, food processing, alcohol or the use of non-steroidal anti-inflammatory drugs (NSAIDs), asymptomatic LTP-sensitised patients may develop symptoms. Co-factor-induced anaphylaxis has readily been described.

#### *Clinical application*

It is often difficult to decide whether a positive LTP IgE is clinically relevant and so a careful history, including potential co-factor exposure, should always be sought. However, a negative Pru p 3 IgE virtually excludes LTP sensitisation. Allergen exposure could be reduced by peeling peaches and apples, as the LTP concentration of peach skin is seven-fold higher than that of the pulp.<sup>13</sup> The seeds of fruits should also be avoided, as should foods produced from processes where whole fruit is crushed.

#### PATHOGENESIS-RELATED PROTEIN 10 (PR-10)

One of the major plant-derived allergens, PR proteins, are

induced by plants as a defence mechanism, and they exhibit anti-fungal, anti-bacterial, insecticidal, nematocidal and antiviral activities. The amino acid homologues of PR proteins are responsible for the cross-reactivity among allergens from diverse plants. Many of the PR proteins could possibly be food, latex and pollen allergens.

Pollen-related food syndrome (latex–fruit syndrome) and birch-mugwort-celery-spice syndrome can be explained by the cross-reactivity between different PR proteins. South Africans are not as sensitised to birch pollen as individuals from Central Europe, which was also reflected in our data demonstrating Bet v 1 sensitisation levels of approximately 2%. There is a paucity of data on the primary sensitising pollen responsible for PR protein sensitisation in South Africa. This could possibly be attributed to the PR proteins in maize pollen, but unfortunately maize pollen components are not currently available for commercial use.

It was interesting that we could demonstrate that 8% of patients were sensitised to kiwi thaumatin-like protein (Act d 2), a PR-5 protein. Symptomatic kiwi allergy is not reported frequently in South Africa. More research should be conducted to identify the primary sensitiser of PR protein allergy in South Africa, specifically thaumatin-like protein (Act d 2), and the possible role of maize pollen and local grass pollens in sensitisation.

Often organically grown, pesticide-free plants would produce higher levels of PR proteins and may be more allergenic to sufferers of PR protein allergy. It is also intriguing to note that PR proteins are integral to disease resistance in genetically modified (GM) plants and are also used as preservative agents. The enhanced expression of PR proteins in GM plants may be associated with increased allergenicity. Various guidelines are defined by the Food and Agriculture Organization (FAO), the World Health Organization (WHO) and the Codex Alimentarius Commission (Codex) for determining whether a new GM crop can be commercialised; however, testing for allergenicity is not part of these guidelines.<sup>3</sup>

#### *Clinical application*

PR-10 proteins are localised mostly to the pulp of fruit. Patients may test positive on allergen-specific IgE to wheat, peanut and soya due to PR-10 sensitisation. As symptoms upon ingestion are often mild and limited to the oral cavity, it is important to identify PR-10 as the source of sensitisation to avoid unnecessary dietary elimination. PR-10 proteins are heat-labile and degrade after processing, therefore dietary advice could include the use of cooked or processed foods, which may be tolerated.

Because PR-10 allergy may cause more severe symptoms than profilin allergy, a careful history should be taken and food challenges performed when these are clinically indicated. PR-10 allergens may be present in higher concentrations in some organic and some GM foods; therefore, this should be incorporated in clinical history-taking and patient advice.

## **OTHER CROSS-REACTIVE PROTEIN FAMILIES REPRESENTED IN ISAC**

### SERUM ALBUMIN

Serum albumin is found in fluids and tissues, as is seen in cow's milk (Bos d 6), blood, beef and dander. Cross-reactivity between various mammal species may be explained by the positivity to

serum albumin – for example, cat (Fel d 2), dog (Can f 3) and horse (Equ c 3) dander.

#### *Clinical application*

Serum albumins are sensitive to heat and digestion. Consequently, patients may tolerate well-cooked foods containing albumins. Serum albumin sensitisation to dog, cat or horse is not an indication for immunotherapy for inhalant allergens for furry animals.

#### TROPOMYOSINS

Tropomyosins are proteins found in the muscle fibres of different species and are responsible for the cross-reactivity between invertebrates (eg HDM (Der p 2), shrimp (Pen m 1), German cockroach (Bla g 7) and Herring worm (Ani s 3)).

#### *Clinical application*

Because tropomyosin is resistant to heat and digestion, reactions to cooked foods are possible and severe systemic reactions occur regularly. Patients sensitised to tropomyosin only do not respond well to HDM immunotherapy and should therefore not be considered for immunotherapy.

#### LIPOCALINS

Lipocalins are stable proteins and important allergens in furry animals. Cross-reactivity between various furry animals may frequently be present.

#### *Clinical application*

If immunotherapy is considered, it is important to establish the primary sensitiser – for example, dog (Can f 1, Can f 2), cat (Fel d 2), mouse (Mus m 1) and horse (Equ c 3).

#### PARVALBUMINS

Parvalbumin is the major allergen in fish (Gad c 1) and is resistant to heat and digestion; therefore, reactions to cooked foods are possible.

#### *Clinical application*

Patients could experience only mild symptoms such as oral allergy syndrome (OAS), but severe and systemic reactions may also occur.<sup>14</sup> The parvalbumin content of different fish

species may vary, with swordfish and tuna generally having a lower content. A good history, prick–prick testing with specific fish species, and food challenges may be indicated to manage patients appropriately.

#### **LIMITATIONS OF THIS STUDY**

This study was performed on sequential patients referred for ISAC testing and was not corrected for the geographic diversity of sample origins. We are aware that there are some regional differences in inhalant allergen sensitisation in South Africa; accordingly, it may be possible that the sensitisation data may not be equally representative of all the geographic regions in South Africa.<sup>4</sup>

The data collected in this study were based on the original allergen component ISAC assay. The allergen composition of this original ISAC assay has subsequently changed, which has meant that more recent data could not be included in this study as a direct comparison. The microarray platform currently available has changed in the following ways:

- Components added are Der p 23 (HDM), Can f 4 (dog-specific lipocalin) and Can f 6 (dog lipocalin), Alpha-gal (red meat allergen), Ana 0 3 (cashew nut storage protein) and Cor a 14 (hazel nut storage protein).
- Components which were removed from the ISAC include Pla a 2 (Plane tree) and Jug r 2 (Walnut) due to their cross-reactivity to CCD, and also bee (Api m 1, Api m 4) and wasp (Pol d 5 and Ves v 5) venom components, which can be ordered separately on singleplex assays (Immunocaps).

#### **CONCLUSION**

This study contributes to our understanding of allergen sensitisation patterns in South Africa by adding component sensitisation data to our current diagnostic knowledge pool. This raises awareness of the extent of allergen component cross-reactivity in South Africa, which can contribute to the optimal diagnosis and management of allergic patients in South Africa.

#### **DECLARATION OF CONFLICT OF INTEREST**

The authors declare no conflict of interest.

This article has been peer reviewed.

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