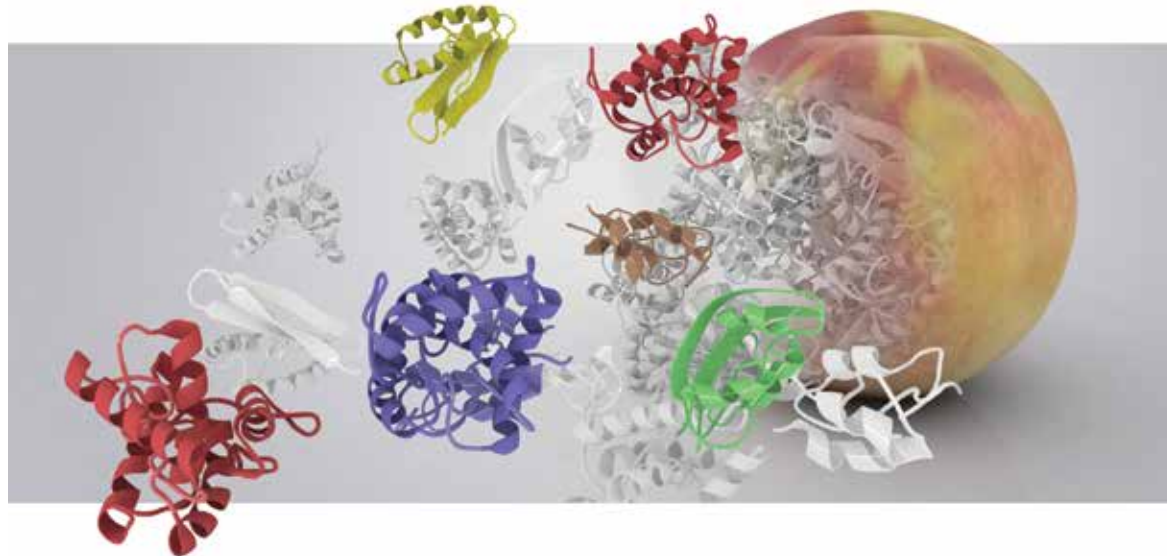


A Clinical Reference Guide to Molecular Allergy

Go Molecular!

1. Molecular Allergy – The Basics

Further information about molecular allergy and the interactive allergy component identification and interpretation tool can be found from **AllergyEducation.co.uk** and **AllergyEducation.ie**



Preface

Molecular allergens have been described in scientific literature for well over a decade now, but it has only been in recent years that they have been used more routinely in the allergy clinic.

New technology can be challenging and it often requires a period of adjustment and adaptation. There are many allergen components covering many different sources and their clinical relevance is continually emerging year on year. This can make it difficult to remember their relevance. Many clinicians have commented to me that they could do with a simplified 'all in one guide' so I have tried to simplify molecular allergy based on the components Thermo Fisher Scientific has in its portfolio.

The intention of part 1 in this guidebook series is to give a basic introduction to molecular allergy focusing on plant food allergy, although other molecular sources such as venoms and aeroallergens are also discussed. This guide gives an introductory overview of the important themes within molecular allergy, especially protein families, their clinical relevance and nomenclature. If there is one important aspect to learn in molecular allergy it is the scientific relevance of protein families, as they are the key to understanding clinical molecular allergy.

A straightforward summary of the main allergen components, what ImmunoCAP products are available and interpreting test results can be found in part 2 of this series – 'The Allergen Components'. I hope you find this guidebook series useful.

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Thermo Fisher Scientific



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Go Molecular! Molecular allergens tell us more

Until recently, the main diagnostic tools in IgE mediated allergy have been clinical history, allergen provocation, skin prick and specific IgE blood tests. Molecular allergy brings a new level of understanding which is changing practice as physicians seek to improve on existing diagnostic technologies.

Molecular allergy is the field of allergy diagnosis that investigates protein allergens at molecular level. Therefore instead of investigating the “sum” of all allergen proteins in whole allergens e.g. peanut, important individual proteins within a peanut can be investigated for specific IgE sensitisation. IgE antibody profiles to these molecules vary significantly from patient to patient and they also differ geographically, due to local differences of exposure.

Molecular diagnostics reveal more factual information about what a patient is allergic to, as individual proteins and profiles can indicate different clinical characteristics.

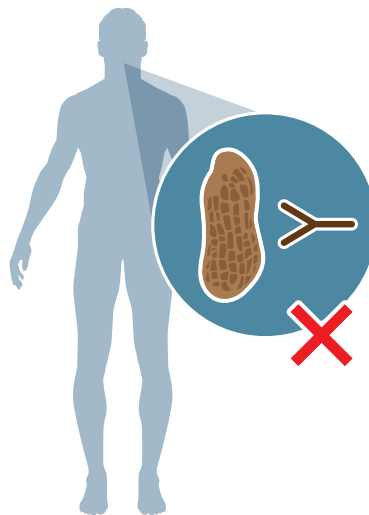


Figure 1: Illustration of the common misconception that there is one IgE antibody produced by the human body for a whole peanut allergen

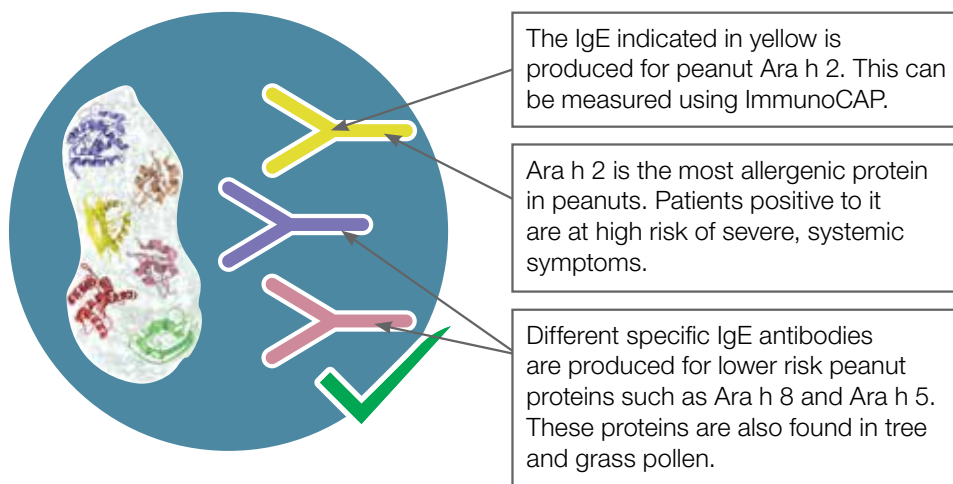


Figure 2: Illustration of the reality that there are lots of different IgE antibodies produced which bind to specific individual molecular proteins in peanut, like Ara h1, Ara h 2 and Ara h 8.

Ara h 2 is an allergen protein resistant to metabolic change and it seems to have the highest allergenic potential from all proteins in peanut. You can measure different antibodies produced by patients in response to different molecular proteins by using ImmunoCAP components. IgE antibodies are useful measurements of a patient's immunological response in their current allergy status. High levels to Ara h 2 will often indicate a patient at high risk of severe, systemic symptoms if peanuts are eaten.

Clinical utility

Allergen component diagnostics measure IgE to particular allergen components, uncovering additional information about an underlying allergy. Not only do they indicate specific allergen reactivity in the way that whole extracts do but they are also indicators for:

1. Understanding patient risk – add confidence to your assessment
2. Selecting patients for immunotherapy – useful for venom and aeroallergy patient selection
3. Understanding cross-reactions between species – help to understand multiple sensitisations e.g. in pollen-food syndrome

The intention of this first guide book is to give the physician, dietician or scientist a background to molecular allergy. A straightforward summary of allergen components and interpretation of the results can be found in part 2 of this series.

Much of the clinical value of molecular allergen testing up to now has been demonstrated within food allergy, especially within plant foods such as nuts, fruits and legumes. Therefore the majority of information in this reference guide focuses on food allergen components, although a brief overview of other allergen components which provide clinical value, such as those from pollens, latex and insect venoms, is included.

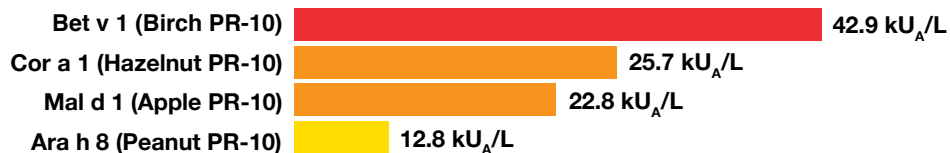
Component families

By introducing molecular allergy into your daily practice you will soon change your paradigm of thinking from that of single source allergens to diverse component families.

In molecular allergy, understanding the significance of protein families from protein sources is an important leap of knowledge in terms of scientific understanding.

Component families referred to in this guide are families with similar functions and structures found in many allergen sources. For example, plants contain storage proteins such as vicilins, transport proteins such as lipid transport proteins and defense proteins such as PR-10s (pathogenesis-related family number 10 proteins).

To begin with, below is an example of a patient's IgE test results with suspect plant food allergy:



The above test results could be interpreted in three different ways:

- Traditional thinking: four different specific IgE reactions to four different plant sources
- On a molecular level: IgE to one protein family group i.e. PR-10 allergy – also indicating cross-reactive IgE
- The patient is also likely to be sensitised to other PR-10 proteins not measured (you couldn't measure them all!). The above is representative of PR-10 sensitisation as a whole and may be relevant to the patient's clinical history to other allergens, e.g. almond contains PR-10 proteins
- This same way of thinking can be applied to profilin or LTP (lipid transfer protein) profiles for example. So you have estimates of results also for sources not tested and this is a fundamental paradigm change in allergy practice

More on protein families and their clinical relevance will be discussed later in this guide.



Interpretation of results

In this guide, interpretation has been simplified as much as possible in terms of presence of IgE. The presence of allergen-specific IgE is usually a risk of allergy symptoms and **a result ≥ 0.1 kUA/L indicates sensitisation**. Traditionally, the higher the IgE level the greater the risk. Some molecular allergens are associated with a higher risk for systemic reactions, whilst some allergens are considered at no or a very low risk for severe reactions. A high level IgE to a high-risk allergen such as Ara h 2 or Cor a 9 would often carry a high risk for patients.

Always consider tests results in association with a clinical history.

Further reading

- Garcia BE, Lizaso MT. Cross-reactivity Syndrome in Food. *Allergy* 2011;21(3):162-170.
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Allergen component nomenclature – The WHO/IUIS Committee

Allergen and allergen components are identified and categorised by a joint partnership of The World Health Organization (WHO) and The International Union of Immunological Sciences (IUIS). The WHO/IUIS Allergen Nomenclature Sub-committee is responsible for maintaining and developing a unique, unambiguous and systematic nomenclature for allergenic proteins. The systematic nomenclature is based on the Linnaean system and is applied to all allergens. For further information check the IUIS allergen nomenclature website at www.allergen.org

Allergen components are given an abbreviation based on the Latin name of the allergen source (the first three letters of the first word and first letter of the second). The allergen protein is also given a number based on the order of discovery (when registered/ approved by the IUIS committee). An example of peanut allergen component nomenclature is below, referring to Ara h 2:

Peanut – ***Arachis hypogaea*** – Ara h 2

Phadia AB, the leading manufacturer of allergen components, also gives the test a prefix 'n' for native sourced allergen proteins or an 'r' for recombinant sourced allergen proteins that are used in the IgE tests.

You can look up all identified allergens at www.allergome.org

Other clinical considerations

Allergen load

Of course, always think about the patient's clinical history – the most important part of allergy diagnosis. Taking detailed information from a patient such as their lifestyle and what they eat is essential. Molecular testing will reveal crucial data but it will never replace a good clinical history. From the patient's clinical history you will discover how much of each food allergen they have been eating, for example. Consuming large amounts of allergens at a time such as when quickly drinking a soy milk drink can affect a patient's symptom outcome. Even normally harmless allergens such as PR-10 proteins consumed in great amounts can provoke more serious allergy symptoms in some patients (such as drinking soy milk).

A patient could be sensitised to several allergens, and also to several allergen components within one allergen source. This will contribute to the overall allergen load.¹ For example if a patient is positive to multiple peanut storage components such as Ara h 1, Ara h 2 and Ara h 3, they are likely to have a higher IgE load and are therefore possibly at more risk for severe reactions than someone who is monosensitised.²⁻⁴



Diagnostic performance

ImmunoCAP components contain pure proteins, measure only IgE to single molecules and give easy-to-understand results.

Whole extract-based tests contain all, or at least most, relevant allergen molecules from an allergen source (e.g. peanut) and measure the sum of multiple IgEs which gives high sensitivity but sometimes can create difficulties in interpretation of results.

Components therefore have technical diagnostic superiority at measuring important individual IgEs of interest such as Ara h 2 in peanut or Cor a 9 in hazelnut. They simply measure IgE specific to one protein and offer reliable results in terms of minimal variation – the same as all ImmunoCAP products. However, it must be remembered that a component test only measures one type of IgE and that a patient will often have IgE antibodies to several molecules contained in the specific allergen source.

As such, it is recommended that you request testing for the whole allergens and ask the laboratory to test for components if the whole allergen is positive.

Food allergy, the food matrix and what we eat

Food is made up of complex matrices of natural constituents such as proteins, fats and carbohydrates. The way that the human body processes food creates by-products of the original food structure. The natural state of proteins can be changed even before we eat them, most obviously by cooking but also by storage and processing e.g. liquidising or concentrating (as for fruit juices).

There are many different metabolic processes that occur as soon as food enters the digestive system. Enzymatic action starts straight away in the mouth; heat and gastric juices play a role as food enters the stomach and further activity is then concentrated in the gut until the food is absorbed. Overall – countless interactions between food and biological processes.

Fats are metabolised into products such as fatty acids. Carbohydrates are broken down eventually into sugars. Most allergens are proteins, made up of amino acid chains and peptides, and within these structures are regions called epitopes. It is these recognition sites that specific IgE molecules bind to. This can lead to histamine release and other mediator release, resulting in allergy symptoms.

Molecules of high allergenic potential

Some molecular proteins are more resistant than others to metabolic change, due to strong 3D chemical structures; e.g. storage proteins from peanut (Ara h 1, Ara h 2 and Ara h 3) or ovomucoid from hen's egg (Gal d 1). It is these tough allergens that have higher resistance to digestion. Therefore their allergenic potential is higher as their epitope structures remain intact. As a result, these proteins can cause more systemic symptoms than unstable proteins (Figure 3).

Molecules of low allergenic potential

Cross-reactive allergen molecules such as PR-10s and profilins (present in nuts, fruits and pollen) are more fragile in structure and therefore susceptible to digestive processes of heat and enzyme activity. Fragile proteins start to break down in the mouth which can cause less problematic reactions such as oral allergy syndrome (OAS). As the epitope binding regions in these proteins is destroyed, these molecules don't tend to induce such an aggressive IgE response.

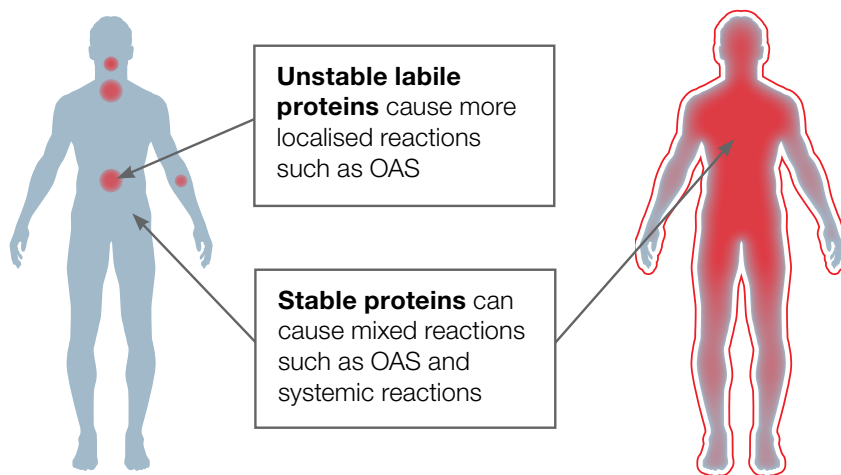


Figure 3: An overview of the biological differences in how proteins can cause different symptoms in the human digestive tract

Allergen profile variability

If molecules vary in their potential to trigger allergy it raises the question:

Q: 'If a patient is IgE tested using a whole extract (the source) how do you know which proteins within the source they are sensitised to?'

A: 'The simple answer is that a whole extract test does not provide all the answers!'

The above question and answer is quite thought-provoking. A whole extract IgE test (the source) is a mixture of lots of individual proteins. It would be impossible to tell which molecular proteins a patient is IgE positive to unless they were separated individually – as they are in ImmunoCAP allergen components. Also, all patients vary in which components they are sensitised to and their molecular profiles therefore vary significantly.

Going molecular by using ImmunoCAP molecular components puts a large portfolio of different allergen components at your disposal. By selecting allergen components you can build individual patient profiles, improving diagnostic clarity and the ability to convey factual information. In ImmunoCAP ISAC you have an allergen profile producer that measures components from 51 sources (representative for approximately 90% of clinical allergen sources). More on ISAC can be found in the third guide book in this series.

Patients testing positive to a whole extract (e.g. positive skin prick test to peanut or serum IgE to peanut) can be positive to either allergen proteins of high allergenic potential or of low/no allergic potential. By using allergen component diagnostics it is possible to better differentiate between them i.e. put patients into low- and high-risk groups.

Unfortunately, mixed forms of allergy exist as of course a patient can be genuinely sensitised to high-risk allergens and low-risk allergens, and can also have more varied symptoms such as OAS together with systemic symptoms.

Furthermore, in a given situation a lot of other factors such as stress, amount of allergen, ongoing infections etc, have an impact on the actual clinical reaction.

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- Breitender H and Mills CEN. Plant food allergens and functional aspects of allergenicity. *Biotechnol Adv* 2005;23:395-399.
- Hauser M, *et al.* Panallergens and their impact on the allergic patient. *Allergy, Asthma Clin Immunol* 2010;6:1.

Specific and cross-reactive allergens

Cross-sensitisation of whole allergens

As you have seen, molecular allergens can be split into allergens of high and low potential for clinical symptoms, and these allergens can be further grouped as being molecules specific to the source or molecules that can be cross-reactive. Identifying these molecules helps us to better understand the characteristics of an individual's allergy.

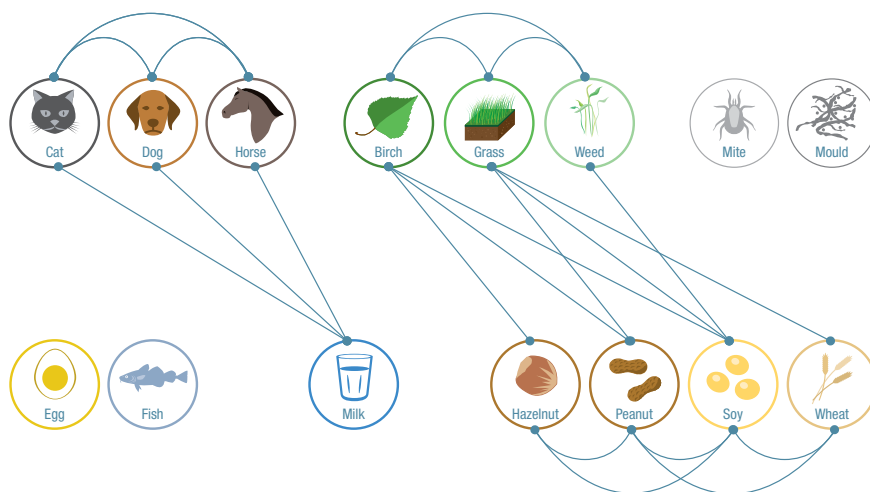


Figure 4: Illustration of a typical UK allergen profile

The above figure demonstrates a typical UK allergen test panel. Many of the allergens could experience IgE cross-reactions. For instance dog, cat and horse all contain the family lipocalin and also serum albumin which is contained in milk. Birch, grass and weed contain profilins, which are also found in the legumes soy and peanut, as well as wheat and hazelnut. IgE cross-reactions can confound results, although ImmunoCAP components can be used to improve diagnostic clarity.

Specific components are more or less unique to their source, whilst cross-reactive allergens can be found in even distantly related species. You can learn more about the significance of these types of allergens at:

AllergyEducation-MA.com

This website contains an educational course which describes the basics of molecular allergy and includes patient case examples.

Specific allergens and primary food allergy

Identifying IgE to specific molecules often indicates the cause of allergy symptoms. In food allergy, the allergens that initially trigger the immune system to produce specific IgE antibodies are often referred to as **primary allergens**. Mostly these are food proteins more resistant to digestion, which therefore are likely to **provoke systemic allergy symptoms**.

Secondary reactions and pollen-food syndrome

Cross-reactive allergens with much conserved structures between different species (so-called “pan-allergens”) can be found in plants, but some are also found in other, not closely related sources, including venoms, fish, mites and shrimp. For example dust mite and shrimp share a cross-reactive risk protein called tropomyosin. In plants in particular, panallergens are very widespread even in distantly related species such as between celery and birch trees.

In plant food allergy, pan-allergens are often the culprits for much asymptomatic or symptomatic sensitisation. IgE antibodies primarily targeted towards proteins in pollen (e.g. Birch Bet v 1) cross-react to similar proteins in food, causing a broad “secondary” sensitisation profile. Within clinical allergy this is often referred to as **pollen-food syndrome** and in the context of latex – **latex-fruit syndrome**.

Cross-reactive allergens can produce allergy symptoms which are **sometimes mild**, but the primary sensitiser should always be sought after. Therefore using a range of specific and cross-reactive allergen component tests it is possible to differentiate primary and secondary reactions.

Further reading

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- Zuidmeer L and van Ree R. Lipid transfer protein allergy; primary allergy/food syndrome in some cases. *Curr Opin Clin Immunol* 2007;7:269-273.
- Santos A and van Ree R. Profilins: Mimickers of Allergy or Relevant Allergens? *Int Arch Allergy Immunol* 2011;155:191-204.
- Fernández-Rivas M, et al. Allergies to fruits and vegetables. *Pediatr Allergy Immunol* 2008;19:675-681.



Plant components

Plant component families are shared between species; the closer the species are related the more similar the components can be. This increases the potential for IgE molecules directed against pollen allergen epitopes to bind to similar allergen epitopes in food. This immunological mechanism is often the cause for broad sensitisation patterns seen in many allergic patients. The two dominant sensitising plant aeroallergens in Northern Europe are pollens from timothy grass and birch trees. Both of these species are culprits for much of the seasonal hay fever symptoms that appear in the UK every spring (birch) and summer (timothy grass). These pollens contain many cross-reacting proteins such as PR-10 proteins and profilin.

There are five main types of plant component groups indicated in allergy. These are PR-10, Profilin, LTPs, Storage Proteins and CCDs which are explained in more detail below. Further references regarding plant food proteins can be found towards the back of this guide.

Storage proteins

Storage proteins are biological reserves of nutrients and amino acids used by organisms to grow. They are found in plants such as seeds and nuts, and proteins with corresponding functions can be found in mammals such as those in egg whites (e.g. ovalbumin) or milk (casein). Storage proteins are structurally complex and commonly regarded as much more stable to heat and proteases compared to allergens such as PR-10s and profilins. There is evidence that the 2S albumin (e.g. Ara h 2) is one of the most stable plant food molecules and therefore the most clinically important. The Ara h 2 molecules are not easily destroyed by gastric fluid and thus will be immunologically functional in the gastrointestinal tract with the potential to trigger systemic reactions such as asthma, urticaria, angioedema or anaphylaxis.⁵ Storage proteins are more or less specific to their source and do not cross-react except for very closely related allergen sources (e.g. between legumes such as soy and peanut).

LTPs (Lipid Transfer Proteins)

LTPs are very stable small molecules widespread in plant food such as fruits, nuts and vegetables. They are found concentrated in the skin of Rosaceae fruits especially in the fuzz of peach – the pulp contains less of the allergen. LTPs are pan-allergens and highly cross-reactive. IgE sensitisation to LTPs has been mostly described in southern Europe, in patients with severe reactions to peach and other fruits belonging to the Rosaceae family (pear, cherry, apple etc.). LTP allergy has also been described in legumes such as peanut, as well as hazelnut.

The LTP sensitisation pattern in northern Europe is not completely understood and is documented more in southern Europe. The protein characteristics of LTPs explain their clinical relevance due to their high resistance to heat and protease digestion. LTP molecules are quite resistant to gastric fluid and thus will be immunologically functional in the gastrointestinal tract with the potential to trigger systemic reactions. LTPs are also associated with local reactions including OAS.

PR-10 (Pathogenesis-Related family number 10) proteins

Plant defence proteins such as PR-10s are concentrated in the pulp of fruit, but they can also be found in pollen. Bet v 1 PR-10 is the major allergen in birch pollen and is highly similar to other PR-10 proteins in other plant food such as Rosaceae fruits (peach, apple and cherry etc.), as well as in nuts and legumes.

In a typical birch allergy scenario, birch pollen causes sensitised patients to become primary sensitised to PR-10 proteins. This can cause typical hay fever-like symptoms such as an itchy/blocked nose, runny eyes etc.

As a further consequence, patients who eat PR-10 proteins found in nuts or fruit can react due to IgE cross-reactions. Food allergy caused via cross-reactivity is sometimes referred to as secondary food allergy. Again this is likely to result in local symptoms such as OAS, but depending on the amount of the cross-reactive protein more severe reactions may also occur (e.g. Gly m 4 induced soy milk reactions).

Profilin proteins

Profilin proteins occur in many different plant species and cause broad sensitisation patterns. They are found for example in pollen (e.g. birch or grass), fruit (Rosaceae: apple, cherries) and vegetables, nuts and latex. It has been proposed that just one profilin from one plant species is enough for testing IgE sensitisation to profilin, due to the large similarity and cross-reactivity of this protein group. Profilins from birch (Bet v 2) and/or timothy grass (Phl p 12) are often used in measuring IgE to profilin. Profilins are sensitive to heat and proteases and will thus primarily give rise to OAS as the clinical manifestation of food allergy. It is widely accepted that profilins have less clinical relevance than PR-10 proteins, although in some cases profilin sensitisation may cause severe reactions.

CCDs (Cross-reactive Carbohydrate Determinants)

Some molecular structures such as CCDs are shared between many species and can be found in insect venoms, pollens and plant foods. CCDs are not proteins but carbohydrate chains (glycan side chains attached to amino acid structures). The clinical impact of IgE to CCDs is considered very low although positive IgE test results are frequent. Again, by using a molecular approach this can be easily established and patients' management tailored to their results.

Equally CCDs help us to understand polysensitisation to multiple plant foods and latex or double positivity between bee and wasp venoms. It is also worth noting that most plant allergen extract preparations from natural sources contain CCD molecules (as they do at the source), whilst recombinant sources are CCD-free and hence more specific.

Interpreting results from cross-reactive protein families

Example 1

You could use a variety of ImmunoCAP component tests when resolving a birch-food allergic patient. Is it a true food allergy? Bet v 1 PR-10 is a dominating primary allergen of a birch-allergic patient. Bet v 1 could produce cross-reactions between other plant food species. The example below demonstrates a patient profile of PR-10 sensitisation with a suspected case of IgE-mediated peanut allergy. For the purposes of this example all other risk allergens such as Ara h 2 in peanut or Cor a 9 from hazel nut were IgE-negative.



Like all ImmunoCAP specific IgE tests, allergen components give results in kU_A/L (ImmunoCAP ISAC gives results in ISU). Primary sensitising allergens from within the same protein family (in this example PR-10 protein family) will normally give the highest specific IgE level. Other secondary IgE sensitisations will give similar specific IgE readings but normally lower levels than the primary sensitising allergen due to reduced protein homology (and therefore reduced IgE binding).

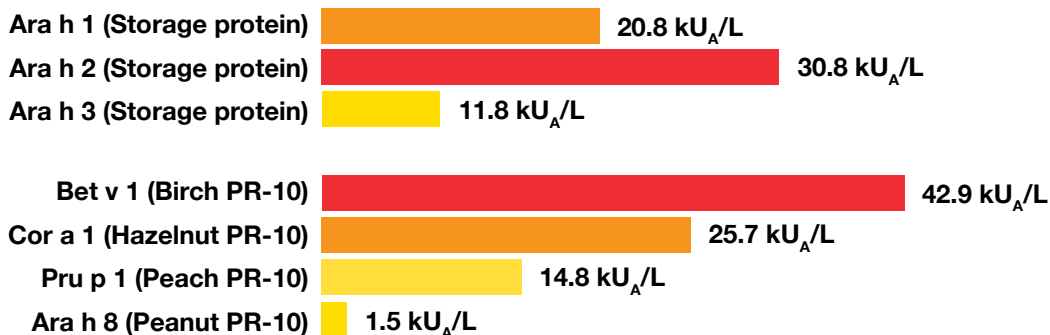
Clinical interpretation:

- Food-pollen syndrome caused by a primary PR-10 birch-related pollen allergy
- Likely symptoms local/mild or none e.g. oral allergy to hazelnut, peach and peanut

“Secondary” reactions due to cross-reactivity can occur via plant allergens such as CCDs and profilins. On the other hand if a patient is allergic to primary molecular proteins that don't cross-react (such as storage proteins) then this serves as a diagnostic marker of risk which is covered further in this guide.

Example 2

Using the previous example of suspected peanut allergy the IgE results could have looked like this:



Clinical interpretation:

- Primary sensitisation to peanut allergens Ara h 1, Ara h 2 and Ara h 3
- Ara h 2 is the most important peanut allergen; the patient is at high risk of severe, systemic symptoms
- The patient also has concomitant birch sensitisation and perhaps other allergy symptoms such as rhinitis, asthma and oral itching
- Food pollen syndrome – caused from a primary PR-10 birch-related pollen allergy. Likely reactions to these foods are local/mild or none e.g. oral allergy
- Overall mixed allergy might occur – both systemic and local symptoms

References and further reading on the plant proteins can be found at the back of this book.

Always use the results in combination with a clinical history. IgE presence always implies risk.

Summary of plant components

Plant protein families are shared between species; the closer the species are related the more similar the proteins can be. This increases the potential for IgE molecules directed against pollen allergen epitopes to bind to similar allergen epitopes in food. There are five main types of plant protein groups indicated in allergy. These are storage proteins, nsLTP, PR-10, profilin proteins and CCDs (cross-reactive carbohydrate determinants):

Protein family	Risk for systemic reactions?	Do I have to consider many different allergen sources?
Storage proteins	Yes. Storage proteins are heat and digestion stable which explains their ability to more often cause systemic reaction in addition to OAS.	No. Storage proteins are not cross-reactive, except for very closely related allergen sources (e.g. between legumes such as soy and peanut).
nsLTP	Yes. nsLTPs are heat and digestion stable which explains their ability to more often cause systemic reaction in addition to OAS.	Yes. Partly cross-reactive (the degree of structural similarity varies between nsLTPs in plant food and pollen).
PR-10	Low. Often cause only local symptoms such as OAS due to their sensitivity to heat and digestion, but a few cases with systemic reactions have been reported e.g. for soy Gly m 4 and Celery Api g 1.	Yes. Partly cross-reactive (the degree of structural similarity varies between PR-10 in plant food and birch-related pollen).
Profilin	Low. Often have little clinical relevance in allergic diseases. However, profilins may cause local reactions in some patients allergic to plant foods including citrus fruits, banana and tomato, and a few cases with systemic reactions have been reported e.g. for melon and lychee.	Yes. Highly cross-reactive (high degree of structural similarity between profilins in pollen, plant food and latex).
CCD	Very low. Usually not associated with clinical reactions but may induce IgE antibody responses in some patients.	Yes. Highly cross-reactive (same CCD structure in pollen, plant food and venoms).

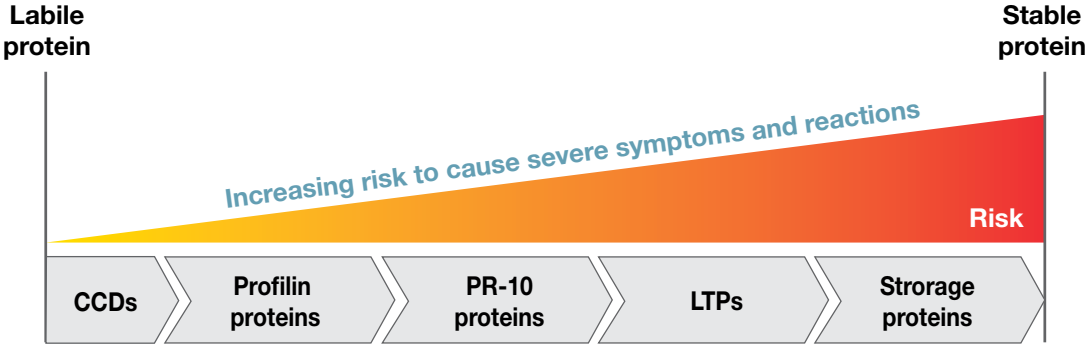


Figure 5: Illustration of level of risk associated with common plant component families

Plant components in common foods and pollens

Component family/ allergen source	Prolifin	PR-10	LTP	Storage proteins				
Birch	Bet v 2	Bet v 1						
Timothy grass	Phl p 12							
Latex	Hev b 8		Hev b 12					
Apple	Mal d 4	Mal d 1	Mal d 3					
Cherry	Pru av 4	Pru av 1	Pru av 3					
Almond	Pru d 4	Pru du 1	Pru du 3	Pru du 2s	Pru du 11S			
Apricot		Pru ar 1	Pru ar 3					
Peach	Pru p 4	Pru p 1	Pru p 3					
Pear	Pyr c 4	Pyr c 1	Pyr c 3					
Raspberry	Rub i 4	Rub i 1	Rub i 3					
Strawberry	Fra a 4	Fra 1	Fra a 3					
Peanut	Ara h 5	Ara h 8	Ara h 9	Ara h 1	Ara h 2	Ara h 3	Ara h 6	Ara h 7
Soy	Gly m 3	Gly m 4		Gly m 5	Gly m 6			
Hazelnut	Cor a 2	Cor a 1	Cor a 8	Cor a 9	Cor a 14			
Brazil Nut				Ber e 1	Ber e 2			
Walnut	Jug r 5		Jug r 3	Jug r 1	Jug r 2	Jug 4		
Pistachio				Pis v 1	Pis v 2	Pis v 3	Pis v 5	
Cashew				Ana o 1	Ana o 2	Ana o 2	Ana o 3	
Sesame	Des i 8			Ses i 1	Ses i 2	Ses i 3	Ses i 6	Ses i 7
Wheat*	Tri a 12		Tri a 14	Tri a 19	Gliadin			
Barley	Hor v 12		Hor v 14	Hor v 21	Hor v 36			
Maize	Zea m 12		Zea m 14	Zea m G1	Zea m G2			
Rice	Ory s 12		Ory s 14	Iry s 19kd	Ory s 36	Ory s GLP52	Ory s GLP63	
Carrot	Dau c 4	Dau c 1	Dau c 3					
Cabbage	Bra o 8		Bra o 3					
Tomato	Lyc 1	Lyc 4	Lyc e 3	Lyc e 7S	Lyc e 11S			
Melon (musk)	Cuc m 2	Cuc m 3						
Celery	Api g 4	Api g 1	Api g 2 and 6					

	Plant food not associated with storage proteins unless found in the seed
	Grasses do not contain PR-10 proteins
	Available plant food ImmunoCAP allergen components
	Protein not formally identified but likely
	No storage proteins associated with this allergen source

*Wheat – Tri a 19 and gliadin are storage proteins but belong to a different family to, for example, LTPs or 2S albumins – they belong to the cereal prolamin family

Other allergen components

Molecular allergens also provide useful information from non-plant sources such as venoms from stinging insects. Below is a brief overview, although further information on clinical interpretation and what ImmunoCAP components are available can be found in guidebook 2 – ‘The Allergen Components’. The below is intended as an introduction to other allergen component areas, including a few references for further reading.

Allergens from non-plant sources

Egg and milk

Dairy products such as milk and egg are associated more with paediatric allergy which children tend to outgrow at a young age. However, in a recent longitudinal egg allergy study in the UK, Clark *et al.* showed that many children don't outgrow their egg allergy until well past 5 years old, in fact the median age in this study was 10 years of age for egg allergy resolution.⁶

Egg and milk contain allergen components that are likely to be linked to more severe symptoms; these allergens are resistant to metabolic change (hen's egg Gal d 1 Ovomucoid; cow's milk, Bos d 8 Casein). Therefore patient groups negative to these tests have been observed to tolerate cooked forms of the allergen. Conversely persistent allergy is associated with the same epitopes, which again can be used as risk markers.

Further reading

- Ando H, *et al.* Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. *J Allergy Clin Immunol* 2008; 122:583-588.
- Alessandari C, *et al.* Ovomucoid (Gal d 1) specific IgE detected by microarray system predict tolerability to boiled hen's egg and an increased risk to progress to multiple environmental sensitisation. *Clin and Exp Allergy* 2012;42(3):441-450.
- Fiocchi A, *et al.* Molecular diagnosis of cow's milk allergy. *Curr Opin Allergy Clin Immunol* 2011;11:216-221.
- Nowak-Węgrzyn A, *et al.* Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol* 2008;122:342-347.

Parvalbumins

Cyp c 1 (carp, oily fish) and Gad c 1 (cod, white fish) are both major fish allergen proteins and markers for fish IgE sensitisation. Parvalbumins are expressed in lower levels in certain fish species such as tuna, swordfish and some mackerel and this perhaps explains why fish-allergic patients can sometimes tolerate these species. Using ImmunoCAP Cyp c 1 and Gad c 1 gives broad spectrum coverage of the parvalbumins family and IgE analysis of fish. A negative result to both tests in a patient investigated for food allergy would inform the clinician of potential low risk of oral challenge and/or lead to further investigations for other possible culprit allergens.

Further reading

- Garcia BE and Lizaso MT. Cross-reactivity Syndromes in Food Allergy. *J Investig Allergol Clin Immunol* 2011;21(3):162-170.
- Sharp MF and Lopata AL. Fish Allergy in Review. *Clin Rev Allerg Immunol* 2013; Epub ahead of print.
- Sastre J. Molecular diagnosis in allergy. *Clin Exp Allergy* 2010;40(10):1442-1460.



Tropomyosins

Tropomyosin proteins are highly cross-reactive actin-binding proteins located in muscle fibres amongst many invertebrate species such as shrimps (Pen a 1), dust mite (Der p 10), cockroach (Bla g 7) and other crustacean foods such as crab, lobster and mollusc. Therefore tropomyosin is an allergen that can be both inhaled and ingested. About 10% of dust mite-allergic patients have IgE to tropomyosin. Some studies suggested that exposure to dust mite tropomyosin may sensitise against shrimp tropomyosin.

Further reading

- Leung NYH, *et al.* Current Immunological and Molecular Biological Perspectives on Seafood Allergy: A comprehensive review. *Clin Rev Allerg Immunol* 2012; Epub ahead of print.
- Gamez C, *et al.* Tropomyosin IgE positive results are a good predictor of shrimp allergy. *Allergy* 2011;66:1375-1383.

Latex

True latex allergy can be identified using specific markers as much cross-reactivity is caused by the profilin allergen Hev b 8 and also CCDs. The association of latex allergy and allergy to plant-derived foods is called latex-fruit syndrome. An increasing number of plant sources, such as avocado, banana, chestnut, kiwi, peach, tomato, potato and bell pepper have been associated with this syndrome.

IgE antibodies to Hev b 1 and Hev b 3 are considered specific markers for latex allergy especially in multi-operated children/patients. IgE to Hev b 5 and Hev b 6 are mainly associated with occupational exposure to latex e.g. in healthcare workers and food-handling personnel using latex gloves. Hev b 8 the profilin and Hev b 6.02 can be used for examining cross-reactivity. If an exclusive sensitisation to latex profilin (Hev b 8) occurs, then clinically relevant allergic symptoms are hardly to be expected. Further information on latex markers can be found in part 2 of this series.

Further reading

- Garnier L, *et al.* Molecular allergens in the diagnosis of latex allergy. *Eur Ann Allergy Clin Immunol* 2012;44(2):73-79.
- Schuler S, *et al.* Microarray-based component-resolved diagnosis of latex allergy: isolated IgE-mediated sensitization to Latex profilin Hev b 8 may act as confounder. *Clin Transl Allergy* 2013;3:11.

Immunotherapeutics – Aeroallergens

Understanding cross-sensitisation and identifying the right allergen source

Clinically it is obviously important to select the correct patients for the right aero-immunotherapy and this is not always easy. Patients can be cross-sensitised to several plant species; therefore sometimes it is not clear what the disease-eliciting source is. Molecular allergen tests can help streamline the identification process. Specific molecules from, for example, grass species can differentiate and identify true grass-allergic patients.

Determining a patient's molecular profile will also help to indicate if they are likely to respond satisfactorily to immunotherapy. Immunotherapy products vary from manufacturer to manufacturer; they contain molecules from the allergen source but which ones and in what quantity? Most immunotherapies contain larger quantities of the major allergens such as Bet v 1 in birch and Phl p 1 and Phl p 5 in timothy grass. Much lower quantities of the minor allergens are included. Patients who are positive only to the minor allergens are less likely to respond to immunotherapy satisfactorily since the treatment extracts sometimes contain low amounts of these allergens. For example the patient might be sensitised to Phl p 7 or Phl p 12 which are present in low and variable amounts in grass immunotherapy products.

Sander *et al.*⁷ explored the relationship between Phl p 5 content of grass skin prick extracts and different sublingual immunotherapies.⁷ The study data showed quite a variance of content of Phl p 5 in skin prick test solutions. Phl p 5 content varied from 15-427 µg/mL. Whereas Phl p 5 content in immunotherapeutics ranged from 0.2-21.6 µg/mL. There is more information regarding immunotherapy in the second part of this mini-series of guidebooks.

Further reading

- Focke M, *et al.* Heterogeneity of commercial timothy grass pollen extracts. *Clin Exp Allergy* 2008;38(8):1400-1408.
- Focke M, *et al.* Molecular composition and biological activity of commercial birch pollen allergen extracts. *Eur J Clin Invest* 2009;39(5):429-436.
- Schmid-Grendelmeier P. Recombinant Allergens – Routine diagnostics or still only science? *Der Hautarzt* 2010;61(11):946-953.

Immunotherapeutics – Venoms

Many patients with suspected venom allergy can be positive for both bee and wasp whole allergens. Using specific markers for wasp (Ves v 1 and Ves v 5) and bee (Api m 1) it is possible to differentiate patients before selecting the right immunotherapeutic solution. Double positivity can be caused by CCDs. ImmunoCAP recombinant venom components are CCD-free which enables an allergist to distinguish between positivity from cross-reactions and true venom allergy.

Further reading

- Mittermann I, *et al.* Recombinant allergen-based IgE testing to distinguish bee and wasp allergy. *J Allergy Clin Immunol* 2010;125(6):1300-1307.
- Muller U, *et al.* IgE to recombinant allergens Api m 1, Ves v 1 and Ves v 5 distinguish double sensitisation from cross-reaction in venom allergy. *Allergy* 2012;67:1069-1073.

Available ImmunoCAP allergen components

The term 'allergen component' is used for products based on molecular allergens purified from either their natural source (native) or biotechnologically produced as recombinant proteins.

By using tests for single allergenic components as a complement to more traditional IgE antibody tests, further clinically relevant information can be gained.

ImmunoCAP allergen components are useful tools when investigating and explaining allergic reactions more in detail and to determine if they are caused by cross-reacting IgE antibodies to different allergens.

Allergen components, native and recombinant

Product		Code	Size	Art. No.	Barcode
Grass pollens					
nCyn d 1 Bermuda grass	<i>Cynodon dactylon</i>	g216	10	14-4972-01	CFA
rPhl p 1 Timothy	<i>Phleum pratense</i>	g205	10	14-5234-01	BSU
rPhl p 2 Timothy	<i>Phleum pratense</i>	g206	10	14-5235-01	C0K
nPhl p 4 Timothy	<i>Phleum pratense</i>	g208	10	14-5288-01	C0L
rPhl p 6 Timothy	<i>Phleum pratense</i>	g209	10	14-5289-01	BSV
rPhl p 7 Timothy	<i>Phleum pratense</i>	g210	10	14-5290-01	BSW
rPhl p 11 Timothy	<i>Phleum pratense</i>	g211	10	14-5291-01	BSX
rPhl p 12 Profilin, Timothy	<i>Phleum pratense</i>	g212	10	14-5292-01	BSY
rPhl p 1, rPhl p 5b Timothy	<i>Phleum pratense</i>	g213	10	14-5312-01	BU1
rPhl p 7, rPhl p 12 Timothy	<i>Phleum pratense</i>	g214	10	14-5313-01	BU2
rPhl p 5b Timothy	<i>Phleum pratense</i>	g215	10	14-5338-01	BV3
Weed pollens					
nAmb a 1 Ragweed	<i>Ambrosia elatior</i>	w230	10	14-4969-01	CF8
nArt v 1 Mugwort	<i>Artemisia vulgaris</i>	w231	10	14-4970-01	CF9
nArt v 3 LTP, Mugwort	<i>Artemisia vulgaris</i>	w233	10	14-4983-01	CJ2
rPar j 2 LTP, Wall pellitory	<i>Parietaria judaica</i>	w211	10	14-5311-01	C2M
nSal k 1 Saltwort	<i>Salsola kali</i>	w232	10	14-4978-01	CFE
rPla l 1 Plantain	<i>Plantago lanceolata</i>	w234	10	14-5751-01	D1H

Product		Code	Size	Art. No.	Barcode
Tree pollens					
rBet v 1 PR-10, Birch	<i>Betula verrucosa</i>	t215	10	14-5225-01	BPV
rBet v 2 Profilin, Birch	<i>Betula verrucosa</i>	t216	10	14-5226-01	BR1
rBet v 4 Birch	<i>Betula verrucosa</i>	t220	10	14-5287-01	BT7
rBet v 6 Birch	<i>Betula verrucosa</i>	t225	10	14-5345-01	CF1
rBet v 2, rBet v 4 Birch	<i>Betula verrucosa</i>	t221	10	14-5310-01	BU0
nCup a 1 Cypress	<i>Cupressus arizonica</i>	t226	10	14-4977-01	CFD
rOle e 1 Olive	<i>Olea europaea</i>	t224	10	14-5705-01	CTC
nOle e 7 LTP, Olive	<i>Olea europaea</i>	t227	10	14-4993-01	CKT
rOle e 9 Olive	<i>Olea europaea</i>	t240	10	14-4999-01	CTZ
rPla a 1 London plane	<i>Platanus acerifolia</i>	t241	10	14-5957-01	D2H
Microorganisms					
rAlt a 1	<i>Alternaria alternata</i>	m229	10	14-5346-01	CE0
rAsp f 1	<i>Aspergillus fumigatus</i>	m218	10	14-5293-01	BPL
rAsp f 2	<i>Aspergillus fumigatus</i>	m219	10	14-5294-01	BPM
rAsp f 3	<i>Aspergillus fumigatus</i>	m220	10	14-5295-01	BT4
rAsp f 4	<i>Aspergillus fumigatus</i>	m221	10	14-5296-01	BPH
rAsp f 6	<i>Aspergillus fumigatus</i>	m222	10	14-5297-01	BPP
Epidermals and animal proteins					
nBos d 6 BSA, Cow	<i>Bos spp.</i>	e204	10	14-5009-01	BRV
rCan f 1 Dog	<i>Canis familiaris</i>	e101	10	14-4955-01	CBN
rCan f 2 Dog	<i>Canis familiaris</i>	e102	10	14-4956-01	CBP
nCan f 3 serum albumin Dog	<i>Canis familiaris</i>	e221	10	14-5241-01	C14
rCan f 5 Dog	<i>Canis familiaris</i>	e226	10	14-4998-01	CMZ
rFel d 1 Cat	<i>Felis domesticus</i>	e94	10	14-4905-01	BY0
rFel d 4 Cat	<i>Felis domesticus</i>	e228	10	14-5702-01	CT9
rEqu c 1 Horse	<i>Equus caballus</i>	e227	10	14-5700-01	CN7
nFel d 2 serum albumin Cat	<i>Felis domesticus</i>	e220	10	14-5240-01	BRX
nSus s Pig albumin, Swine	<i>Sus scrofa</i>	e222	10	14-5242-01	C36
Mites					
nDer p 1 House dust mite	<i>Dermatophagoides pteronyssinus</i>	d202	10	14-4966-01	CFG
rDer p 2 House dust mite	<i>Dermatophagoides pteronyssinus</i>	d203	10	14-4967-01	CG2
rDer p 10 Tropomyosin, House dust mite	<i>Dermatophagoides pteronyssinus</i>	d205	10	14-4985-01	CG5



Product		Code	Size	Art. No.	Barcode
Venoms					
rApi m 1 Phospholipase A2, Honey bee	<i>Apis mellifera</i>	i208	10	14-4987-01	CJ7
rVes v 1 Phospholipase A1, Common wasp	<i>Vespula vulgaris</i>	i211	10	14-4995-01	CMR
rVes v 5 Common wasp	<i>Vespula vulgaris</i>	i209	10	14-4992-01	CJ8
rPol d 5 Paper wasp	<i>Polistes dominulus</i>	i210	10	14-4994-01	CJ09
Occupational					
rHev b 1 Latex	<i>Hevea brasiliensis</i>	k215	10	14-5324-01	C20
rHev b 3 Latex	<i>Hevea brasiliensis</i>	k217	10	14-5326-01	C2A
rHev b 5 Latex	<i>Hevea brasiliensis</i>	k218	10	14-5327-01	C1Z
rHev b 6.01 Latex	<i>Hevea brasiliensis</i>	k219	10	14-5328-01	C28
rHev b 6.02 Latex	<i>Hevea brasiliensis</i>	k220	10	14-5329-01	C22
rHev b 8 Profilin, Latex	<i>Hevea brasiliensis</i>	k221	10	14-5330-01	C1V
rHev b 9 Latex	<i>Hevea brasiliensis</i>	k222	10	14-5331-01	C2C
rHev b 11 Latex	<i>Hevea brasiliensis</i>	k224	10	14-5333-01	C29
Occupational / Enzymes					
Alkalase	<i>Bacillus spp.</i>	k205	10	14-5126-01	C1F
nAna c 2 Bromelain, Pineapple	<i>Ananas comosus</i>	k202	10	14-5127-01	BT1
nAsp o 21 alpha-amylase	<i>Aspergillus oryzae</i>	k87	10	14-5370-01	595
nCar p 1 Papain, Papaya	<i>Carica papaya</i>	k210	10	14-5130-01	BT0
nGal d 4 Lysozyme, Egg	<i>Gallus spp.</i>	k208	10	14-5128-01	C0T
Maxatase	<i>Bacillus licheniformis</i>	k204	10	14-5128-01	C2F
Savinase	<i>Bacillus spp.</i>	k206	10	14-5132-01	C2R
nSus s Pepsin, Swine	<i>Sus scrofa</i>	k213	10	14-5258-01	C3B

Product		Code	Size	Art. No.	Barcode
Foods					
rAct d 8 PR-10, Kiwi	<i>Actinidia deliciosa</i>	f430	10	14-4984-01	CG7
rAna o 3 Cashew nut	<i>Anacardium occidentale</i>	f443	10	14-5760-01	D0W
rApi g 1.01 PR-10, Celery	<i>Apium graveolens</i>	f417	10	14-4957-01	CBR
rAra h 1 Peanut	<i>Arachis hypogaea</i>	f422	10	14-4963-01	CDF
rAra h 2 Peanut	<i>Arachis hypogaea</i>	f423	10	14-4964-01	CDG
rAra h 3 Peanut	<i>Arachis hypogaea</i>	f424	10	14-4965-01	CDH
rAra h 8 PR-10, Peanut	<i>Arachis hypogaea</i>	f352	10	14-5341-01	CEZ
rAra h 9 LTP, Peanut	<i>Arachis hypogaea</i>	f427	10	14-4980-01	CFC
rBer e 1 Brazil nut	<i>Bertholletia excelsa</i>	f354	10	14-5343-01	CDS
nBos d 4 alpha-lactalbumin, Milk	<i>Bos spp.</i>	f76	10	14-4522-01	CTP
nBos d 5 beta-lactoglobulin, Milk	<i>Bos spp.</i>	f77	10	14-4523-01	CTR
nBos d 8 Casein, Milk	<i>Bos spp.</i>	f78	10	14-4524-01	CTS
nBos d Lactoferrin, Milk	<i>Bos spp.</i>	f334	10	14-5253-01	C16
rCor a 1 PR-10, Hazel nut	<i>Corylus avellana</i>	f428	10	14-4981-01	CFB
rCor a 8 LTP, Hazel nut	<i>Corylus avellana</i>	f425	10	14-4968-01	CDP
nCor a 9, Hazel nut	<i>Corylus avellana</i>	f440	10	14-5758-01	D0M
rCor a 14, Hazel nut	<i>Corylus avellana</i>	f439	10	14-5754-01	CZP
rCyp c 1 Carp	<i>Cyprinus carpio</i>	f355	10	14-5344-01	CF0
rGad c 1 Cod	<i>Gadus morhua</i>	f426	10	14-4971-01	CEY
nGal d 1 Ovomucoid, Egg	<i>Gallus spp.</i>	f233	10	14-4805-01	904
nGal d 2 Ovalbumin, Egg	<i>Gallus spp.</i>	f232	10	14-4804-01	903
nGal d 3 Conalbumin, Egg	<i>Gallus spp.</i>	f323	10	14-5222-01	C18
rGly m 4 PR-10, Soy	<i>Glycine max</i>	f353	10	14-5340-01	CDR
nGly m 5 beta-conglycinin, Soy	<i>Glycine max</i>	f431	10	14-4990-1	CLV
nGly m 6 Glycinin	<i>Glycine max</i>	f432	10	14-4991-01	CLU
rJug r 1 Walnut	<i>Juglans regia</i>	f441	10	14-5762-01	D0T
rJug r 3 LTP, Walnut	<i>Juglans regia</i>	f442	10	14-5954-01	D11
rMal d 1 PR-10, Apple	<i>Malus domestica</i>	f434	10	14-5703-01	CWR
rMal d 3 LTP, Apple	<i>Malus domestica</i>	f435	10	14-5704-01	CWS
rPen a 1 Tropomyosin, Shrimp	<i>Penaeus aztecus</i>	f351	10	14-5335-01	C11
rPru p 1 PR-10, Peach	<i>Prunus persica</i>	f419	10	14-4960-01	CBV
rPru p 3 LTP, Peach	<i>Prunus persica</i>	f420	10	14-4961-01	CBW
rPru p 4 Profilin, Peach	<i>Prunus persica</i>	d421	10	14-4962-01	CBX
rTri a 14 LTP, Wheat	<i>Triticum aestivum</i>	f433	10	14-5701-01	CN6
rTri a 19 Omega-5 Gliadin, Wheat	<i>Triticum aestivum</i>	f416	10	14-4954-01	C8H
Gliadin		f98	10	14-5752-01	CXG
Miscellaneous					
MUXF3 CCD, Bromelain		214	10	14-5339-01	CJU



Common questions regarding molecular components

What is a molecular allergen-specific IgE test and does it differ technically from normal specific IgE tests that I request from my laboratory?

Technically they work in the same way and give results in kUA/L the same as normal whole extract sources such as cat, peanut etc.

How many ImmunoCAP components are available?

There are currently just over 100 component allergens in the product range. There is a list included in this guide.

For each allergen source how do I know that the allergen components available represent the whole allergen extract?

The components that are selected are generally considered the most clinically important ones, as defined by current scientific studies. For example there are over 30 proteins reported in the peanut extract, many not clinically relevant or with unknown relevance. For technical reasons we cannot produce all the components that are needed but the number will increase. Thermo Fisher Scientific develops between 4-8 new components every year. Since today all components are not available as single tests it is suggested to use the available components together with the whole extract to cover the spectrum of patients' sensitisations. Like genetic science, the field of molecular allergy is ever-expanding as we gain further scientific information and knowledge.

What is ImmunoCAP ISAC?

ImmunoCAP ISAC is a microarray chip which tests for 112 allergen components simultaneously. It is a multiplex test and produces a report on a patient's allergen component profile. It has been found useful for the following but this list is not exhaustive: complex allergy, OAS, and cases of multi-sensitisation, idiopathic anaphylaxis and high total IgE patients. Further information on ImmunoCAP ISAC is in the third mini guide of this series.

Where can I get access to ImmunoCAP ISAC?

Your local immunology laboratory should be able to refer your sample for testing, therefore contact your local lab to find out what is possible.

Is it possible to have a whole extract test negative and component to be positive?

This is possible in some cases. The whole extract is a mass of mixed proteins represented in the test as it is within its natural composition at the source. The allergen component is a pure protein of only one type with no interference from other proteins. Overall we consider the component tests as an advancement of technology over whole extract tests giving more specificity and sometimes even more sensitivity. Using a combination of both whole extract and components (where possible) is currently considered the best strategy for diagnosis.

Glossary

Allergen component – single allergy-provoking molecular protein from an allergen source e.g. Ara h 2 from a whole peanut extract.

Cross-reactivity/Cross-sensitisation – IgE antibodies produced to one allergen may cross-react to other allergens from botanically related and/or structurally similar sources. Cross-reactive antibodies can cause a variety of different clinical outcomes.

Epitope – the amino acid sequence of a protein corresponding to the allergen-binding part of the IgE antibody (Fab). Determinant is another name.

ImmunoCAP – an *in vitro* test for the measurement of IgE antibodies. ImmunoCAP is the most used blood test in this area and is regarded as the gold standard. ImmunoCAP is also available for testing for other immunoglobulins (e.g. IgA/ IgG).

Panallergen – evolutionarily conserved and widely distributed allergen, ubiquitous component of several complex sources of allergens. IgE antibodies to a panallergen may cross-react with homologous allergens and thus also give rise to symptoms to many different allergens in a patient.

Primary sensitising allergen – an allergen originally triggering the immune system to produce specific IgE antibodies. For example Bet v 1 from birch or Ara h 2 from peanut.

Minor and major allergens – often you find references and descriptions of major and minor allergens. Major allergen components are allergens that account for over 50% of sensitisation within an allergy. Minor allergens are often less prevalent in triggering allergy. For instance in birch allergy the major allergen is Bet v 1 (PR-10), whilst a minor allergen is Bet v 2 (profilin).

Secondary allergen – an allergen that has a similar structure to a primary sensitising allergen and that cross-reacts with IgE. This occurs in food-pollen syndrome for example, when an individual is sensitised to birch PR-10 (Bet v1) and the IgE antibodies then cross-reacts to peanut PR-10 (Ara h 8).

Whole allergen extract – refers to the crude mixture of proteins that is obtained from an allergen source (e.g. birch pollen or peanut)



Educational resources

- Website: **AllergyEducation.co.uk** – Thermo Fisher Scientific educational website explaining the basics of Molecular Allergy and interactive tool to help with identification of relevant components and interpretation
- Website: **AllergyEducation-MA.com** – Thermo Fisher Scientific educational training course exploring the basics of Molecular Allergy
- Canonica GW, *et al.* A WAO – ARIA – GA2LEN consensus document on molecular-based allergy diagnostics. *World Allergy Organ J* 2013;6(1):17.
- Thermo Fisher Scientific – Cross-reactivity in plant food allergy – A focused book on cross-sensitisation
- Thermo Fisher Scientific – Native and cross-reactive allergen components – A more detailed book giving an overview of allergen components
- Thermo Fisher Scientific – Individual literature packs on various components are available. Educational PowerPoint slide sets are also available. Please contact Thermo Fisher Scientific if you would like a set:

– Egg	– Milk	– Birch
– Grass	– Hazelnut	– Peanut
– Wheat	– Soybean	– Venoms
– Apple	– Walnut	– Cashew

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Recommended literature

PR-10 proteins

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CCDs

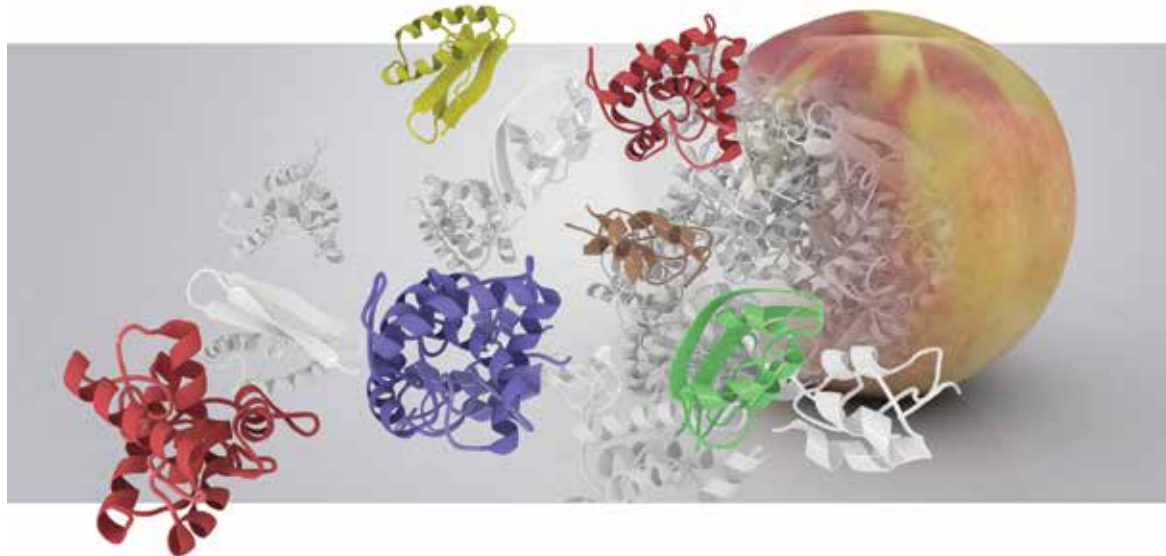
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A Clinical Reference Guide to Molecular Allergy

Go Molecular!

2. The Allergen Components

Further information about molecular allergy and the interactive allergy component identification and interpretation tool can be found from **AllergyEducation.co.uk** and **AllergyEducation.ie**



**Allergy
Education**

www.AllergyEducation.co.uk
www.AllergyEducation.ie

 **ImmunoCAP®**
Is it allergy?

Preface

Molecular allergens have been described in scientific literature for well over a decade now, but it has only been in recent years that they have been used more routinely in the allergy clinic.

New technology can be challenging and it often requires a period of adjustment and adaptation. There are many allergen components covering many different sources and their clinical relevance is continually emerging year on year. This can make it difficult to remember their relevance. Many clinicians have commented to me that they could do with a simplified 'all in one guide' so I have tried to simplify molecular allergy based on the components Thermo Fisher Scientific has in its portfolio.

The intention of this reference book is to give a straightforward summary of the main allergen components, what ImmunoCAP products are available, and interpreting test results. I hope you find this guide book useful.

Neal Bradshaw BSc (Hons)

**Molecular Allergy Specialist
Immunodiagnosics
Thermo Fisher Scientific**



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Foreword

Component resolved diagnostics is a relatively new concept and has taken allergy into the 21st century allowing better understanding of clinical cross-reactions and beginning to allow us to explain some of the symptoms that we see clinically.

This simple-to-read quick reference guide on component technology allows you to understand what is becoming an essential part of the modern allergy diagnostic armoury. There are helpful introductions explaining the nomenclature and in which groups of patients the allergen has importance. This is followed by a simple guide to interpreting results for all the main allergen groups for which these tests have become available. In some areas their use has already become clear and has affected patient treatment, and with this guide the benefits of these breakthroughs will become more widely available.

Dr. Lee Noimark

Consultant Paediatric Allergist

June 2013



As it is adopted into the allergy work-up, molecular allergy is opening new doors that are changing patient management. By using molecular allergens it is possible to understand more about the underlying allergies and add another tool to the diagnostic armoury. Molecular tests are not magic bullets; rather they are an enhancement over conventional extract tests, giving more factual information. The results have to be interpreted like any other specific IgE test and cannot be solely relied upon to determine a diagnosis; results should be used in conjunction with an allergy-focused clinical history.

Molecular allergy testing helps in:

1. Understanding patient risk – adding confidence to your assessment
2. Selecting patients for immunotherapy – useful for venom and aeroallergy patient selection
3. Understanding cross-reactions between species – helping to understand multiple sensitisations e.g. in pollen food syndrome

Many ImmunoCAP allergen components are available in our product range and familiarity with them is essential to understand their clinical implications. To help you implement component testing we have developed a web tool to help you choose which components to select and determine the clinical implications of the results.

This can be also found at:

AllergyEducation.co.uk

The tests themselves are not technically different to other specific IgE tests that are routinely ordered from your lab such as milk, egg, cat or peanut allergens. Extracts like these are made up of lots of different allergen components. Component tests differ as each specific IgE test involves measuring single recombinant or native allergen proteins from a source. For example Pru p 3 is an nsLTP (non-specific lipid transfer protein) from peach.

There is more information on the basics of molecular allergy to be found on our molecular allergy course:

AllergyEducation-MA.com

The purpose of this guide is to offer an 'all in one' reference to each allergen source and its components in a single handy booklet. Molecular allergy involves many different allergen proteins and it can be difficult to remember them all and what the results mean. It is also difficult to remember all the relevant allergen codes, allergen nomenclature, what tests are needed to make an assessment and what is actually available in the product range. I hope this booklet addresses these issues to make life a little easier in the clinic.

What's in this guidebook?

Description, Latin name and allergen nomenclature

Each section of the booklet describes a different allergen source and a little background. A comprehensive list of all of our whole allergens, components and clinical interpretation of the main components can be found at:

AllergyEducation.co.uk

For detailed information on the background of each of our whole allergens and components visit:

Phadia.com/Products/Allergy-testing-products/ImmunoCAP-Allergens

Major and minor allergen components

You will often find references and descriptions for major and minor allergens. Major allergen components are allergens that account for over 50% of sensitisation within an allergy. Minor allergens are often less prevalent in triggering allergy (these are often panallergens which are more likely to cross-react with homologous allergens). For instance in Birch allergy the major allergen is Bet v 1 (PR-10 pathogenesis related family number 10), whilst a minor allergen is Bet v 2 (profilin).

ImmunoCAP IgE test products available and new product updates

Thermo Fisher Scientific strives to develop many clinically relevant components each year. Products available at the time of going to press are listed in each section. If you are interested in the latest updates and product releases register by contacting us at:

Allergy-uk.idd@thermofisher.com

Or through:

AllergyEducation.co.uk

Information given in this guide is for single ImmunoCAP components and is also relevant to whole extract allergens (but not ImmunoCAP ISAC, the array chip; this will be included in the third book of this series). The allergen code is also provided which can be useful when ordering from your local testing laboratory. Whole allergens are still a useful guide and offer value by covering missing components from the source. For example, we currently have five allergen components for peanut but over 15 have been described. We provide the most clinically relevant component tests where possible. We recommend when requesting tests you ask for the whole allergen and ask your laboratory to reflex test for relative components if the whole allergen is positive – the best use of time and resources.

Interpretation of results

In this guide, interpretation has been simplified as much as possible in terms of the presence of IgE. The presence of allergen-specific IgE is usually a risk of allergy symptoms and a result ≥ 0.1 kUA/L indicates sensitisation. Traditionally the higher the IgE antibody level the greater the likelihood of being allergic. Some molecular allergens are associated with a much higher risk, whilst some allergens are considered no or very low risk. A high-titre, high-risk allergen such as Ara h 2 or Cor a 9 would often carry a high risk for patients. Always consider test results in association with a clinical history.

Further reading:

Each section has a further reading suggestion which lists a small number of relevant clinical papers.

Allergen components from plant sources



Plant protein families are shared between species; the closer the species are related the more similar the proteins can be. This increases the potential for IgE antibodies directed against pollen allergen epitopes to bind to similar allergen epitopes in food. There are five main types of allergen groups indicated. These are storage proteins, nsLTP, PR-10, profilin proteins and CCDs (cross-reactive carbohydrate determinants):

Protein family	Risk for systemic reactions?	Do I have to consider many different allergen sources?
Storage proteins	Yes. Storage proteins are heat and digestion stable which explains their ability to more often cause systemic reaction in addition to oral allergy syndrome (OAS).	No. Storage proteins are not cross-reactive, except for very closely related allergen sources (e.g. between legumes such as soy and peanut).
nsLTP	Yes. nsLTPs are heat and digestion stable which explains their ability to more often cause systemic reaction in addition to OAS.	Yes. Partly cross-reactive (the degree of structural similarity varies between nsLTPs in plant food and pollen).
PR-10	Low. Often cause only local symptoms such as OAS due to their sensitivity to heat and digestion, but a few cases with systemic reactions have been reported e.g. for soy Gly m 4 and Celery Api g 1.	Yes. Partly cross-reactive (the degree of structural similarity varies between PR-10 in plant food and birch-related pollen).
Profilin	Low. Often have little clinical relevance in allergic diseases. However, profilins may cause local reactions in some patients allergic to plant foods including citrus fruits, banana and tomato, and a few cases with systemic reactions have been reported e.g. for melon and lychee.	Yes. Highly cross-reactive (high degree of structural similarity between profilins in pollen, plant food and latex).
CCD	Very low. Usually not associated with clinical reactions but may induce IgE antibody responses in some patients.	Yes. Highly cross-reactive (same CCD structure in pollen, plant food and venoms).

Plant components in common foods and pollens

Component family/ allergen source	Prolifin	PR-10	LTP	Storage proteins				
Birch	Bet v 2	Bet v 1						
Timothy grass	Phl p 12							
Latex	Hev b 8		Hev b 12					
Apple	Mal d 4	Mal d 1	Mal d 3					
Cherry	Pru av 4	Pru av 1	Pru av 3					
Almond	Pru d 4	Pru du 1	Pru du 3	Pru du 2s	Pru du 11S			
Apricot		Pru ar 1	Pru ar 3					
Peach	Pru p 4	Pru p 1	Pru p 3					
Pear	Pyr c 4	Pyr c 1	Pyr c 3					
Raspberry	Rub i 4	Rub i 1	Rub i 3					
Strawberry	Fra a 4	Fra 1	Fra a 3					
Peanut	Ara h 5	Ara h 8	Ara h 9	Ara h 1	Ara h 2	Ara h 3	Ara h 6	Ara h 7
Soy	Gly m 3	Gly m 4		Gly m 5	Gly m 6			
Hazelnut	Cor a 2	Cor a 1	Cor a 8	Cor a 9	Cor a 14			
Brazil Nut				Ber e 1	Ber e 2			
Walnut	Jug r 5		Jug r 3	Jug r 1	Jug r 2	Jug 4		
Pistachio				Pis v 1	Pis v 2	Pis v 3	Pis v 5	
Cashew				Ana o 1	Ana o 2	Ana o 2	Ana o 3	
Sesame	Des i 8			Ses i 1	Ses i 2	Ses i 3	Ses i 6	Ses i 7
Wheat*	Tri a 12		Tri a 14	Tri a 19	Gliadin			
Barley	Hor v 12		Hor v 14	Hor v 21	Hor v 36			
Maize	Zea m 12		Zea m 14	Zea m G1	Zea m G2			
Rice	Ory s 12		Ory s 14	Iry s 19kd	Ory s 36	Ory s GLP52	Ory s GLP63	
Carrot	Dau c 4	Dau c 1	Dau c 3					
Cabbage	Bra o 8		Bra o 3					
Tomato	Lyc 1	Lyc 4	Lyc e 3	Lyc e 7S	Lyc e 11S			
Melon (musk)	Cuc m 2	Cuc m 3						
Celery	Api g 4	Api g 1	Api g 2 and 6					

	Plant food not associated with storage proteins unless found in the seed
	Grasses do not contain PR-10 proteins
	Available plant food ImmunoCAP allergen components
	Protein not formally identified but likely
	No storage proteins associated with this allergen source

*Wheat – Tri a 19 and gliadin are storage proteins but belong to a different family to, for example, LTPs or 2S albumins – they belong to the cereal prolamin family



Peanut – *Arachis hypogaea* (Ara h)

Peanut allergy is of great interest in the UK and is a problematic allergen source that over the last decade has increased in prevalence. Peanuts are consumed mainly as peanut butter, as snacks, in confectionery and in baked goods. Peanuts also yield cooking oils (both refined and crude, aromatic and non-aromatic).

It is commonly accepted that Ara h 1, Ara h 2 and Ara h 3 are the major peanut allergens.¹⁻³ These allergens are heat stable and resistant to gastric acid fluid degradation. Ara h 2 is considered to be the most important peanut allergen but IgE also to Ara h 1 and/or Ara h 3 increases risk of severe symptoms.¹⁻⁴ The Ara h 2 allergen component provides the most accurate peanut test in terms of diagnosis.^{1,5-7} Birch pollen allergy patients sensitised to Bet v 1 (PR-10) or Bet v 2 (profilin) can cross-react with Ara h 8 (PR-10) or Ara h 5 (profilin) in peanut respectively. IgE to timothy grass profilin (Phl p 12) can also cross-react with peanut profilin Ara h 5.

Available ImmunoCAP allergen components

Whole Peanut Extract – f13

rAra h 1 – 7S globulin, storage protein – f422

rAra h 2 – 2S albumin, storage protein – f423

rAra h 3 – 11S globulin, storage protein – f434

rAra h 8 – PR-10 protein – f352

rAra h 9 – nsLTP – f427

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to any of the storage proteins Ara h 1, Ara h 2 or Ara h 3 indicates a primary peanut allergy. The patient is at high risk of severe, systemic symptoms, especially if Ara h 2 is positive
- If monosensitised to Ara h 8 then the patient is at risk for local reactions, however, the risk of severe, systemic reactions is low. The patient is more likely to experience local symptoms such as OAS. The patient may be sensitised to other PR-10 containing pollens and plant foods due to cross-reactions
- IgE to Ara h 1, Ara h 2, Ara h 3 and Ara h 8 – mixed forms of allergy may occur including local reactions such as OAS and severe, systemic reactions
- IgE to Ara h 9 nsLTP indicates a risk of both systemic and local reactions. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods

Further reading

- Dang TD, *et al.* Increasing the accuracy of peanut allergy diagnosis by using Ara h 2. *J Allergy Clin Immunol* 2012;129(4):1056-1063.
- Nicolaou N, *et al.* Quantification of specific IgE to whole peanut extract and peanut components in predication of peanut allergy. *J Allergy Clin Immunol* 2011;127(3):684-685.
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Soya Bean – *Glycine max* (Gly m)

Soy is widely used worldwide because it is cheap to produce and because of its high biological value and high quality protein content. It is used as soy protein flour, flakes, concentrates and isolates as well as soy oil. It can be a hidden allergen in processed foods such as meat products, sausages, bakery goods, chocolate and breakfast cereals.

The presence of specific IgE to the Gly m 5 and Gly m 6 indicates real soy allergy and risk of severe systemic reactions.⁸⁻⁹ Gly m 4 (PR-10) is labile to heat, processing and digestion and consumption of processed soy usually causes no or only mild symptoms in Gly m 4 sensitised patients. With unprocessed soy drinks and dietary protein powders (e.g. such as those used in gyms) it is actually possible to ingest a large amount of Gly m 4 at one time, since these products contain high quantities of Gly m 4 that has not been degraded by heat or processing. This can lead to a risk for severe systemic reactions due to high allergen load, especially in pollen-allergic patients during pollen season when there is simultaneous exposure to birch pollen, which contains a cross-reactive PR-10 protein (Bet v 1).¹⁰

Available ImmunoCAP allergen components

Soya Bean – f14

rGly m 4 – PR-10 protein – f353

nGly m 5 – β -conglycinin, storage protein – f431

nGly m 6 – glycinin, storage protein – f432

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- If IgE to either Gly m 5 or Gly m 6 (or both) is present then the patient is at high risk of severe, systemic reactions
- A high allergen load of Gly m 4 can result in systemic symptoms. Therefore even if Gly m 5 and Gly m 6 are IgE negative it is worth checking how much consumption of soy has occurred (the allergen load) especially if the patient is Gly m 4 positive. For example does the patient regularly drink soya milk?
- Gly m 5 and Gly m 6 are often associated with cross-reactions to other similar proteins in other legumes e.g. lentils, and in tree nuts.

Further reading

- Kosma P, *et al.* Severe reactions after the intake of soy drink in birch pollen allergic children sensitised to Gly m 4 *Acta Paediatr* 2011;100:305-307.
- Holzhauser T, *et al.* Soybean (*Glycine max*) allergy in Europe: Gly m 5 (beta-conglycinin) and Gly m 6 (glycinin) are potential diagnostic markers for severe allergic reactions to soy. *J Allergy Clin Immunol* 2009;123(2):452-458.
- Garcia BE and Lizaso MT. Cross-reactivity syndromes in food allergy. *J Investig Allergol Clin Immunol* 2011;21(3):162-170.



Hazelnut – *Corylus avellana* (Cor a)

Hazelnut is widely used and can be a “hidden” allergen; for example as an ingredient in confectionery such as chocolate or nougat. Allergic reactions to hazelnuts range from OAS to severe anaphylactic reactions.¹¹⁻¹²

Cor a 9 and Cor a 14 are both storage proteins which are resistant to digestion and therefore have high allergenic potential to cause systemic symptoms. Presence of specific IgE antibodies to Cor a 8 (nsLTP) is also an indication of severe reactions in patients with a suspected allergy to hazelnut, although nsLTP allergy in northern European countries is less common compared to southern Europe.¹³ In geographical areas in which birch is endemic (including the UK), hazelnut allergy has been mainly associated with cross-reactive IgE to Birch Bet v 1 (PR-10) and Bet v 2 (profilin), which usually causes mild symptoms.¹⁴⁻¹⁷

Available ImmunoCAP allergen components

Whole Hazelnut Extract – f17

rCor a 1 – PR-10 – f428

rCor a 8 – nsLTP – f425

nCor a 9 – 11S globulin, storage protein – f440

rCor a 14 – 2S albumin, storage protein – f439

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to Cor a 9 and/or Cor a 14 indicates a primary hazelnut allergy, the patient is at high risk of severe, systemic allergy
- If IgE to Cor a 1 is present and the other hazelnut components are negative then risk is low for systemic reactions and local symptoms such as OAS are more likely. The patient may be sensitised to other PR-10-containing pollens and plant foods due to cross-reactions
- If IgE to Cor a 8 (nsLTP) is present then mixed allergy is possible, including systemic and local symptoms such as OAS. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods
- If IgE to all hazelnut components is indicated, then mixed forms of allergy are likely such as OAS alongside systemic symptoms

Further reading

- Flinterman AE, *et al.* Lipid transfer protein-linked hazelnut allergy in children from a non-Mediterranean birch-endemic area. *J Allergy Clin Immunol* 2008;121:423-428.
- Verweis MM, *et al.* Young infants with atopic dermatitis can display sensitization to Cor a 9 and 11S legumin-like seed storage protein from hazelnut (*Corylus avellana*). *Paediatr Allergy Immunol* 2011;22:196-201.
- De Knop KJ, *et al.* Age related sensitisation profiles for hazelnut (*Corylus avellana*) in a birch-endemic region. *Paed Allergy Immunol* 2011;22(1 Pt 2):e139-149.
- Masthoff LJ, *et al.* Sensitisation to Cor a 9 and Cor a 14 is highly specific for a hazelnut allergy with objective symptoms in Dutch children and adults. *J Allergy Clin Immunol* 2013;132(2):393-399.

Walnut – *Juglans regia* (Jug r)

Walnut is closely related to the pecan. Walnuts are often eaten as an ingredient in baked goods for instance meat, poultry, fish and pasta dishes or in salads or ice cream. Walnut oil can be allergenic, although this depends on the extraction method and the purity of the end product.⁶⁹

Jug r 1, a storage protein which is resistant to digestion, has a high allergic potential to cause systemic symptoms. Presence of specific IgE antibodies to Jug r 3, an nsLTP, indicates that local symptoms as well as systemic reactions can occur.^{24,70-73}

Available ImmunoCAP allergen components

Whole Walnut Extract – f256

rJug r 1 – 2S albumin, storage protein – f441

rJug r 3 – nsLTP – f442

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to Jug r 1 indicates a primary walnut allergy; the patient is at high risk of severe, systemic reactions
- If IgE to Jug r 3 (nsLTP) is indicated then mixed allergy is possible, involving systemic and local symptoms such as OAS. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods
- Walnut and pecan are closely genetically related and show extensive cross-reactions even between storage proteins^{24,79}

Further reading

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- Rosenfeld L, *et al.* Walnut allergy in peanut-allergic patients: Significance of sequential epitopes of walnut homologues to linear epitopes of Ara h 1, 2 and 3 in relation to clinical reactivity. *Int Arch Allergy Immunology* 2012;157:238-245.



Cashew – *Anacardium occidentale* (Ana o)

The cashew nut comes from the cashew nut tree, a member of the Anacardiaceae family, and is closely related to pistachio. Cashew nut is commonly used as a thickening agent in soups, meats and stews and particularly features in Indian cuisine.

Three storage proteins have been identified so far: Ana o 1, Ana o 2 and Ana o 3 (no nsLTP identified yet). Ana o 3 is a 2S albumin storage protein (the same family as Ara h 2 from peanut) which is resistant to digestion and has a high allergic potential to cause systemic symptoms.^{74,77–78} Significant cross-reactivity has been reported between pistachio nut and cashew nut.^{74–76} Cross-reactivity between cashew nut and walnut is possible, as a result of Ana o 2, the legumin protein which is a major allergen in cashew nut and is also present in walnut.⁷⁴ The cross-reactivity is also suggested by *in vitro* studies.

Available ImmunoCAP allergen components

Whole Cashew Extract – f202

rAna o 3 – 2S albumin, storage protein – f443

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to Ana o 3 indicates a primary cashew allergy; The patient is at high risk of severe, systemic, reactions
- Cashew and pistachio are closely genetically related and show extensive cross reactivity even between storage proteins^{74–76}

Further reading

- Hasegawa M, *et al.* Clinical features of four cases with cashew nut allergy and cross-reactivity between cashew nut and pistachio. *Allergol Int* 2011;60(4):425-432.
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- Roux K, *et al.* Tree nut allergens. *Int Arch Allergy Immunology* 2003;131:234-244.
- Fernandez C, *et al.* Allergy to pistachio: cross reactivity between pistachio nut and other Anacardiaceae. *Clin Exp Allergy* 1995; 25(12):1254-1259.

Stone Fruits – Peach and Rosaceae Family

Due to high structural homology, general stone fruit allergy can be resolved using peach allergen components. In fact Pru p 3 can be a useful general marker for nsLTP allergy in fruit and vegetables due to its cross-reactive nature and high nsLTP levels concentrated in the skin. nsLTPs are highly conserved and widely distributed throughout the plant kingdom.¹⁸⁻²² They have been identified as allergens in the Rosaceae subfamilies of the Prunoideae (peach, apricot, plum) and of the Pomoideae (apple).

Sensitisation to Pru p 3 is associated with systemic symptoms as well as oral allergy.²⁴ Pru p 1 cross-reacts extensively with Bet v 1 homologues from *Prunus* species (e.g. cherry, apricot, plum) and other Rosaceae fruits such as apple and also, and to a lower degree, PR-10 proteins from foods like carrot, celery, soy and peanut.

Available ImmunoCAP allergen components

Stone Fruit Whole Extract – e.g. Almond (f20), Apple (f49), Apricot (f237), Peach (f95), Pear (f94), Plum (f255), Raspberry (f343), Strawberry (o212)
rPru p 1 PR-10 – f419
rPru p 3 nsLTP – f420
rPru p 4 Profilin – f421

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to Pru p 3 (nsLTP): mixed allergy is possible including systemic and local symptoms such as OAS. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods
- If IgE to Pru p 1 and the other peach components are negative then risk is low for systemic reactions and local symptoms such as OAS are more likely. The patient may be sensitised to other PR-10-containing pollens and plant foods due to cross-reactions
- IgE to profilin Pru p 4: low risk, highly cross-reactive. Therefore a high IgE antibody titre result could explain broad sensitisations to other plant proteins that contain profilin, including latex, banana, tomato, potato, avocado, timothy grass, peanut etc

Further reading

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- Rueda M, *et al.* Lipid transfer protein syndrome: clinical pattern, co-factor effect and profile of molecular sensitization to plant-foods and pollens. *Clin Exp Allergy* 2012;42:1529-1539.
- Garcia BE and Lizaso MT. Cross-reactivity Syndromes in Food Allergy. *J Investig Allergol Clin Immunol* 2011;21(3):162-170.



Wheat – *Triticum aestivum* (Tri a)

Wheat is a grass and therefore wheat flour contains many allergen components which are cross-reactive (e.g. profilin) although some are considered as true wheat food allergens. Most wheat allergic patients have IgE antibodies to multiple components both to grass cross-reactive ones and to true food allergens. Gliadins are non-water soluble proteins but are readily dissolved by stomach acid and are considered as true food allergens. Many patients with immediate food wheat allergy are sensitized to the gliadin and/or the nsLTP group of wheat allergens.

IgE antibodies to gliadin (containing α , γ , β and ω gliadins), Tri a 19 (ω -5 gliadin) or Tri a 14 (nsLTP), are associated with allergic reactions to ingested wheat. The wheat proteins, α , γ , β and ω gliadins (especially ω -5 gliadin) have also been reported as major allergens in Wheat – Dependent Exercise-Induced Anaphylaxis (WDEIA).²⁵⁻³¹ Moreover, ω -5 gliadin has been shown to be a specific risk marker in children with immediate allergy to ingested wheat.³²

Available ImmunoCAP allergen components

Wheat whole extract – f4
 α , γ , β and ω gliadins – f98
rTri a 19 ω -5 gliadin – f416
rTri a 14 – nsLTP – f433

Clinical utility

Increasing specificity in wheat food allergy diagnostics, understanding patient risk, an indicator for immediate wheat allergy, detection of wheat-dependent exercise-induced anaphylaxis (WDEIA)

Interpreting the results

- IgE sensitisation to α , γ , β and ω gliadins can indicate immediate wheat food allergy with the patient at high risk of severe, systemic, reactions
- IgE sensitisation to ω -5 gliadin (omega-5) gives even higher specificity than gliadin f98 and is associated with immediate wheat allergy and WDEIA
- ω -5 gliadin has a natural limited presence on the f4 Wheat ImmunoCAP and some wheat allergic patients, especially WDEIA patients, are negative to the f4-test but positive to ω -5 gliadin
- If IgE to Tri a 14 (nsLTP) is present then mixed allergy is possible including systemic and local symptoms such as OAS. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods

Further reading

- Dengsuwan T, *et al.* Wheat ω -5 gliadin is a major allergen in children with immediate allergy to ingested wheat. *J Clin Immunol* 2001;108(4):634-638.
- Ito K, *et al.* IgE antibodies to ω -5 gliadin is associated with immediate symptoms on oral wheat challenge in Japanese children *Allergy* 2008;63:1536-1542.
- Hofmann SC, *et al.* IgE detection to $\alpha/\beta/\gamma$ gliadin and its clinical relevance in wheat-dependant exercise-induced anaphylaxis. *Allergy* 2012;67:1457-1460.

Latex – *Hevea brasiliensis* (Hev b)

Latex allergy can trigger contact urticaria but also severe and even life-threatening allergic reactions. Does the patient have a genuine latex allergy? The association of latex allergy and allergy to plant-derived foods is called latex-fruit syndrome. An increasing number of plant sources such as avocado, banana, chestnut, kiwi, peach, tomato, potato and bell pepper have been associated with this syndrome.

IgE antibodies to Hev b 1 and Hev b 3 are considered markers for latex allergy especially in children who have had multiple operations, such as those with spina bifida (SB).³³ IgE to Hev b 5 and Hev b 6 is mainly associated with occupational exposure to latex e.g. in healthcare workers and food handling personnel using latex gloves.³⁴⁻³⁶ Patients with latex-pollen syndrome are often sensitised to MUXF3 (CCD) and/or Hev b 8 (profilin).³⁷

Available ImmunoCAP allergen components

Latex Whole Extract – K82

rHev b 1 – K215

rHev b 3 – K217

rHev b 5 – K218

rHev b 6.01 – K219

rHev b 6.02 – K220

rHev b 8 – Profilin – K221

MUXF3 – CCD – o214

Clinical utility

Understanding risk and cross-reactions

Interpreting the results

- IgE to Hev b 1, Hev b 3, Hev b 5 or Hev b 6 indicates a risk for genuine latex allergy
- Sensitisation to Hev b 8 and/or MUXF3 and no sensitisation to Hev b 1, Hev b 3, Hev b 5 and Hev b 6 indicates a low risk of latex allergy
- IgE to Hev b 8 only, may indicate latex-pollen syndrome due to cross-reactions with other plants that contain profilin proteins. This does not normally indicate true latex allergy
- IgE to latex Hev b 5 and Hev b 6 is also associated with latex-fruit syndrome (e.g. avocado, kiwi, chestnut or banana)

Further reading

- Ebo DG, *et al.* Component-resolved diagnosis from latex allergy by micro-array. *Clin Exp Allergy* 2010;40(2):348-358.
- Garnier L, *et al.* Molecular allergens in the diagnosis of latex allergy. *Eur Ann Allergy Clin Immunol* 2012;44(2):73-79.
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Hen's egg – *Gallus domesticus* (Gal d)

The total number of egg proteins is not known, but more than 40 have been suggested for egg white alone,³⁹ and up to 24 different antigenic protein fractions have been isolated. Ovomucoid (Gal d 1), ovalbumin (Gal d 2), ovotransferrin/conalbumin (Gal d 3) and lysozyme (Gal d 4) have been identified as the most important allergens in egg white.³⁸ Ovomucoid has been demonstrated to be a major allergen, making up 10% of the egg white protein. Gal d 1 has several important characteristics which make its allergic potential high, such as stability to heat and digestion by proteases. Patients with elevated IgE to ovomucoid are at risk to both raw and cooked egg products.⁴⁰⁻⁴² Specific IgE to Gal d 1 is also a risk factor for persistent hen's egg allergy.⁴³⁻⁴⁵

Available ImmunoCAP allergen components

Egg White Extract – f1
nGal d 1 – ovomucoid – f233
nGal d 2 – ovalbumin – f232
nGal d 3 – conalbumin – f323
nGal d 4 – lysozyme – k208

Clinical utility

Egg allergy persistence, understanding patient risk

Interpreting the results

- IgE sensitisation to Gal d 1 indicates high risk of a persistent egg allergy
- IgE sensitisation to Gal d 1 indicates the patient is at high risk to raw and cooked egg
- IgE sensitisation to Gal d 2, Gal d 3 and Gal d 4 (Gal d 1 negative or low levels) – indicates a risk to raw egg and tolerance to extensively heated egg

Further reading

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Cow's milk – ***Bos domesticus*** (Bos d)

A wide variety of milk protein allergens have been observed giving IgE responses. The major allergens in cow's milk are casein, α -lactalbumin and β -lactoglobulin, although allergens that are present in low quantities, such as Bovine Serum Albumin (BSA) and lactoferrin, are also important since 35-50% of patients are sensitised to these allergens.⁵⁰

Available ImmunoCAP allergen components

Milk allergen – f2

nBos d 4 – α -lactalbumin – f76

nBos d 5 – β -lactoglobulin – f77

nBos d 6 – BSA – e204

nBos d 8 – Casein – f78

nBos d – Lactoferrin – f334

Clinical utility

Milk allergy risk assessment, IgE to casein is an indicator for reactions to cooked milk products and for milk allergy persistence

Interpreting the results

- IgE to Bos d 8 (casein) indicates high risk of milk allergy persistence
- IgE to Bos d 8 (casein) indicates high risk to uncooked and cooked milk products
- IgE negative or low levels of IgE to Bos d 8 and higher levels to either Bos d 4, Bos d 5, Bos d 6 or Lactoferrin indicates a risk for uncooked milk, but a tolerance to cooked milk products is likely

Further reading

- Fiocchi A, *et al.* Molecular diagnosis of cow's milk allergy. *Curr Opin Allergy Clin Immunol* 2011;11:216-221.
- Nowak-Węgrzyn A, *et al.* Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol* 2008;122:342-347.
- Ito K, *et al.* The usefulness of casein-specific IgE and IgG4 antibodies in cow's milk allergic children. *Clin Mol Allergy* 2012;10(1):1.



Tropomyosin

House dust mite – *Dermatophagoides pteronyssinus* (Der p)

Shrimp – *Penaeus aztecus* (Pen a)

Tropomyosin proteins are highly cross-reactive actin-binding proteins located in muscle fibres amongst many invertebrate species such as shrimps (Pen a 1), dust mite (Der p 10), cockroach (Bla g 7) and crustacean foods such as crab, lobster and snails.⁵⁸ Therefore tropomyosin is an allergen that can be inhaled and ingested.

Pen m 1 is heat stable in raw and cooked shrimp.⁵⁷ About 10% of dust mite-allergic patients have IgE to tropomyosin. Some studies suggest that exposure to dust mite tropomyosin may sensitise against shrimp tropomyosin.⁶⁰ Patients with IgE to Der p 10 may potentially have a higher risk of allergic reactions to shellfish (crustaceans and mollusc), insects and parasites.⁵⁹

Available ImmunoCAP allergen components

rDer p 10 – Tropomyosin, House dust mite (*Dermatophagoides pteronyssinus*) – d205

rPen a 1 – Tropomyosin, Shrimp (*Penaeus aztecus*) – f351

Clinical utility

Risk markers, cross-reactive determinations. Specific IgE results to either Pen a 1 or Der p 10 would explain multiple positive results to different shellfish whole extracts

Interpreting the results

- As tropomyosins are highly cross-reactive (and highly homologous) it is possible to use one type of tropomyosin IgE test to measure IgE sensitisation. The results would at least explain sensitisation patterns to numerous invertebrate species including those between mite and shrimp
- IgE to Pen a 1 indicates an allergy risk to different tropomyosins and to crustacean foods in general – cross-reactions through tropomyosin can cause systemic symptoms
- Some patients sensitised to Der p 10 may react to crustacean tropomyosin such as Pen a 1 in shrimp. These patients are at higher risk of crustacean allergy

Further reading

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- Leung NYH, *et al.* Current immunological and molecular biological perspectives on seafood allergy: A comprehensive review. *Clin Rev Allerg Immunol* 2012; Epub ahead of print.

Fish Allergens – Parvalbumins

Cod – *Gadus morhua* – (Gad m)

Carp – *Cyprinus carpio* – (Cyp c)

Parvalbumins are small acidic calcium-binding buffer proteins found in muscle fibres and are the major allergens in fish and amphibians. Parvalbumins are highly cross-reactive. The degree of cross-reactivity is dependent on the degree of protein homology. Parvalbumins proteins have high allergenic potential and are resistant to change even after cooking.

Cyp c 1 (carp, oily fish) and Gad c 1 (cod, white fish) are both major fish allergen proteins and both respective markers for fish IgE sensitisation. Parvalbumins are expressed in lower levels in certain fish species such as tuna, swordfish and some mackerel. This perhaps explains why some fish-allergic patients can tolerate these species.

Recombinant carp parvalbumin was found to contain 70% of the IgE epitopes present in natural extract of cod, tuna and salmon.⁶⁰⁻⁶¹ This suggested that the substance would make a valid tool in the diagnosis of patients with fish allergy.⁶¹ Purified carp parvalbumin has been shown to react with IgE antibodies of more than 95% of individuals allergic to fish, and to contain around 83% of the IgE epitopes present in other fish species.⁶³

Available ImmunoCAP allergen components

rGad c 1 – Cod – f426

rCyp c 1 – Carp – f355

Clinical utility

Understanding risk and cross-reactive determinations

Interpreting the results

- IgE to Cyp c 1 indicates high risk allergy to carp and closely related fish (oily fish) due to cross-reactions
- IgE to Gad c 1 indicates a high risk allergy to cod and closely related fish (white fish) due to cross-reactions
- Using Cyp c 1 and Gad c 1 gives a broad spectrum parvalbumins analysis of white fish and oily fish
- A negative result to both would lead to further investigations

Further reading

- Sastre J. Molecular diagnosis in allergy. *Clin Exp Allergy* 2010;1442-1460.
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Using ImmunoCAP components for aeroallergen immunotherapy; patient selection in birch and grass patients

Timothy Grass – *Phleum pratense* – (Phl p)

Birch – *Betula verrucosa* – (Bet v)

Using ImmunoCAP allergen components it is possible to identify patients who are the most likely to respond to aeroallergen immunotherapy. Immunotherapy vaccines are manufactured to include most major allergens from the sensitisation source.⁶⁴⁻⁶⁵

For example, birch immunotherapy vaccines contain mainly the birch major allergen Bet v 1 (PR-10). This applies to both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT). The exact quantities of allergen present varies from manufacturer to manufacturer.⁶⁴⁻⁶⁵

In some cases a patient may not be positive for the major allergen from the allergen source and is less likely to respond satisfactorily to aeroallergen immunotherapy.⁶⁶ In the case of birch allergy the minor allergens include Bet v 2 (profilin) and Bet v 4 (polcalcin). These are minor pan-allergens and highly cross-reactive and if the patient is sensitised only to these, further investigations may be needed to identify the true allergen source.

The above statements can also be applied to patients selected for grass immunotherapy; in the same way patients can be identified and grouped into how they are likely to respond to immunotherapy. The process for selecting patients for timothy grass and birch allergy immunotherapy is illustrated in the below table:

Available ImmunoCAP allergen components

Timothy Grass	
rPhl p 1	g205
rPhl p 2	g206
nPhl p 4	g208
rPhl p 5b	g215
rPhl p 6	g209
rPhl p 7	g210
rPhl p 11	g211
rPhl p 12 (profilin)	g212
rPhl p 1 + rPhl p 5b	g213
rPhl p 7 + rPhl p 12	g214

Birch	
rBet v 1	t215
rBet v 2	t216
rBet v 4	t220
rBet v 6	t225
rBet v 2 + Bet v 4	t221

Timothy grass and birch aeroallergy – the minor and major allergens

Clinical decision	ImmunoCAP major allergens	ImmunoCAP minor allergens	Interpretational overview
Patient selected for Timothy Grass Immunotherapy	rPhl p 1 + rPhl p 5b (g231*)	rPhl p 7 + rPhl p 12 (g214*)	IgE to major allergens and no IgE to minor allergens – good candidate for specific immunotherapy.
Patient selected for Birch Immunotherapy	rBet v 1 (t215)	rBet v 2 + rBet v 4 (t221*)	IgE to minor allergens and no IgE to major allergens – patient may not respond to specific immunotherapy.

*Indicates dual allergen component

Further reading

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- Focke M, *et al.* Molecular composition and biological activity of commercial birch pollen allergen extracts. *Eur J Clin Invest* 2009;39(5):429-436.
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Using ImmunoCAP components for venom immunotherapy (VIT)

Common wasp – *Vespula vulgaris* – (Ves v)

Honey bee – *Apis mellifera* – (Api m)

Identifying the correct allergen source is highly important for optimising VIT, and ImmunoCAP components can assist diagnosis when patients appear to be IgE test positive to both honey bee and common wasp. Double reactivity to both bee and wasp is not clinically common. In many cases double IgE test positivity can be caused by cross-reactions to CCDs.⁶⁷⁻⁶⁸ Proteins with CCD can be found in many other allergen sources such as plant foods (e.g. peanut) pollens or mites. Recombinant venom components do not carry CCD and therefore provide specificity to the venom diagnostics.

The below decision tree table gives an outline for selecting patients for the correct immunotherapy.

Patients with suspected venom allergy should also be tested for ImmunoCAP tryptase. The patients with high basal levels of tryptase should be investigated for mastocytosis since these patients have higher risk for severe reactions during venom immunotherapy. It is recommended that special attention should be paid to patients who have a basal tryptase measurement of over 10 µg/L.

Available ImmunoCAP allergen components

Honey Bee – rApi m 1 Phospholipase A2, Honey bee – i208

Common Wasp – rVes v 1 Phospholipase A1 – i211

Common Wasp – rVes v 5 – i209

European paper wasp – rPol d 5 – i210

Clinical decision	ImmunoCAP components	Interpretational overview
Venom immunotherapy (patient has double positivity to wasp venom and bee venom)	Ves v 1 + Ves v 5 + Api m 1 + CCD MUXF 3	IgE to Ves v 1, Ves v 5 and no IgE to Api m 1. CCD positive – good candidate for wasp immunotherapy. IgE to Api m 1 and no IgE to Ves v 1 or Ves v 5. CCD positive – good candidate for honey bee immunotherapy. IgE to Ves v 1, Ves v 5 and Api m 1, CCD negative – candidate may need dual immunotherapy to bee and wasp. IgE to CCD and no IgE to Ves v 1, Ves v 5 and Api m 1. Further investigations may be necessary to identify underlying source.

Further reading

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- Muller U, *et al.* IgE to recombinant allergens Api m1, Ves v 1 and Ves v 5 distinguish double sensitisation from cross reaction in venom allergy. *Allergy* 2012;67:1069-1073.
- Ebo DG, *et al.* Component-resolved diagnosis of wasp (yellow jacket) venom allergy. *Clin Exp Allergy* 2013;43(2):255-261.

Allergen components

The term allergen component is used for products based on molecular allergens purified from either their natural source (native) or biotechnologically produced as recombinant proteins.

By using tests for single allergenic components as a complement to more traditional IgE antibody tests, further clinically relevant information can be gained.

ImmunoCAP Allergen components are useful tools when investigating and explaining allergic reactions in detail and to determine if they are caused by cross-reacting IgE antibodies to different allergens.

Product		Code	Size	Art. No.	Barcode
Grass pollens					
nCyn d 1 Bermuda grass	<i>Cynodon dactylon</i>	g216	10	14-4972-01	CFA
rPhl p 1 Timothy	<i>Phleum pratense</i>	g205	10	14-5234-01	BSU
rPhl p 2 Timothy	<i>Phleum pratense</i>	g206	10	14-5235-01	C0K
nPhl p 4 Timothy	<i>Phleum pratense</i>	g208	10	14-5288-01	C0L
rPhl p 6 Timothy	<i>Phleum pratense</i>	g209	10	14-5289-01	BSV
rPhl p 7 Timothy	<i>Phleum pratense</i>	g210	10	14-5290-01	BSW
rPhl p 11 Timothy	<i>Phleum pratense</i>	g211	10	14-5291-01	BSX
rPhl p 12 Profilin, Timothy	<i>Phleum pratense</i>	g212	10	14-5292-01	BSY
rPhl p 1, rPhl p 5b Timothy	<i>Phleum pratense</i>	g213	10	14-5312-01	BU1
rPhl p 7, rPhl p 12 Timothy	<i>Phleum pratense</i>	g214	10	14-5313-01	BU2
rPhl p 5b Timothy	<i>Phleum pratense</i>	g215	10	14-5338-01	BV3
Weed pollens					
nAmb a 1 Ragweed	<i>Ambrosia elatior</i>	w230	10	14-4969-01	CF8
nArt v 1 Mugwort	<i>Artemisia vulgaris</i>	w231	10	14-4970-01	CF9
nArt v 3 LTP, Mugwort	<i>Artemisia vulgaris</i>	w233	10	14-4983-01	CJ2
rPar j 2 LTP, Wall pellitory	<i>Parietaria judaica</i>	w211	10	14-5311-01	C2M
nSal k 1 Saltwort	<i>Salsola kali</i>	w232	10	14-4978-01	CFE
rPla l 1 Plantain	<i>Plantago lanceolata</i>	w234	10	14-5751-01	D1H



Product		Code	Size	Art. No.	Barcode
Tree pollens					
rBet v 1 PR-10, Birch	<i>Betula verrucosa</i>	t215	10	14-5225-01	BPV
rBet v 2 Profilin, Birch	<i>Betula verrucosa</i>	t216	10	14-5226-01	BR1
rBet v 4 Birch	<i>Betula verrucosa</i>	t220	10	14-5287-01	BT7
rBet v 6 Birch	<i>Betula verrucosa</i>	t225	10	14-5345-01	CF1
rBet v 2, rBet v 4 Birch	<i>Betula verrucosa</i>	t221	10	14-5310-01	BU0
nCup a 1 Cypress	<i>Cupressus arizonica</i>	t226	10	14-4977-01	CFD
rOle e 1 Olive	<i>Olea europaea</i>	t224	10	14-5705-01	CTC
nOle e 7 LTP, Olive	<i>Olea europaea</i>	t227	10	14-4993-01	CKT
rOle e 9 Olive	<i>Olea europaea</i>	t240	10	14-4999-01	CTZ
rPla a 1 London plane	<i>Platanus acerifolia</i>	t241	10	14-5957-01	D2H
Microorganisms					
rAlt a 1	<i>Alternaria alternata</i>	m229	10	14-5346-01	CE0
rAsp f 1	<i>Aspergillus fumigatus</i>	m218	10	14-5293-01	BPL
rAsp f 2	<i>Aspergillus fumigatus</i>	m219	10	14-5294-01	BPM
rAsp f 3	<i>Aspergillus fumigatus</i>	m220	10	14-5295-01	BT4
rAsp f 4	<i>Aspergillus fumigatus</i>	m221	10	14-5296-01	BPH
rAsp f 6	<i>Aspergillus fumigatus</i>	m222	10	14-5297-01	BPP
Epidermals and animal proteins					
nBos d 6 BSA, Cow	<i>Bos spp.</i>	e204	10	14-5009-01	BRV
rCan f 1 Dog	<i>Canis familiaris</i>	e101	10	14-4955-01	CBN
rCan f 2 Dog	<i>Canis familiaris</i>	e102	10	14-4956-01	CBP
nCan f 3 serum albumin Dog	<i>Canis familiaris</i>	e221	10	14-5241-01	C14
rCan f 5 Dog	<i>Canis familiaris</i>	e226	10	14-4998-01	CMZ
rFel d 1 Cat	<i>Felis domesticus</i>	e94	10	14-4905-01	BY0
rFel d 4 Cat	<i>Felis domesticus</i>	e228	10	14-5702-01	CT9
rEqu c 1 Horse	<i>Equus caballus</i>	e227	10	14-5700-01	CN7
nFel d 2 serum albumin Cat	<i>Felis domesticus</i>	e220	10	14-5240-01	BRX
nSus s Pig albumin, Swine	<i>Sus scrofa</i>	e222	10	14-5242-01	C36
Mites					
nDer p 1 House dust mite	<i>Dermatophagoides pteronyssinus</i>	d202	10	14-4966-01	CFG
rDer p 2 House dust mite	<i>Dermatophagoides pteronyssinus</i>	d203	10	14-4967-01	CG2

Product		Code	Size	Art. No.	Barcode
Venoms					
rApi m 1 Phospholipase A2, Honey bee	<i>Apis mellifera</i>	i208	10	14-4987-01	CJ7
rVes v 1 Phospholipase A1, Common wasp	<i>Vespula vulgaris</i>	i211	10	14-4995-01	CMR
rVes v 5 Common wasp	<i>Vespula vulgaris</i>	i209	10	14-4992-01	CJ8
rPol d 5 Paper wasp	<i>Polistes dominulus</i>	i210	10	14-4994-01	CJ09
Occupational					
rHev b 1 Latex	<i>Hevea brasiliensis</i>	k215	10	14-5324-01	C20
rHev b 3 Latex	<i>Hevea brasiliensis</i>	k217	10	14-5326-01	C2A
rHev b 5 Latex	<i>Hevea brasiliensis</i>	k218	10	14-5327-01	C1Z
rHev b 6.01 Latex	<i>Hevea brasiliensis</i>	k219	10	14-5328-01	C28
rHev b 6.02 Latex	<i>Hevea brasiliensis</i>	k220	10	14-5329-01	C22
rHev b 8 Profilin, Latex	<i>Hevea brasiliensis</i>	k221	10	14-5330-01	C1V
rHev b 9 Latex	<i>Hevea brasiliensis</i>	k222	10	14-5331-01	C2C
rHev b 11 Latex	<i>Hevea brasiliensis</i>	k224	10	14-5333-01	C29
Occupational / Enzymes					
Alkalase	<i>Bacillus spp.</i>	k205	10	14-5126-01	C1F
nAna c 2 Bromelain, Pineapple	<i>Ananas comosus</i>	k202	10	14-5127-01	BT1
nAsp o 21 alpha-amylase	<i>Aspergillus oryzae</i>	k87	10	14-5370-01	595
nCar p 1 Papain, Papaya	<i>Carica papaya</i>	k210	10	14-5130-01	BT0
nGal d 4 Lysozyme, Egg	<i>Gallus spp.</i>	k208	10	14-5128-01	C0T
Maxatase	<i>Bacillus licheniformis</i>	k204	10	14-5128-01	C2F
Savinase	<i>Bacillus spp.</i>	k206	10	14-5132-01	C2R
nSus s Pepsin, Swine	<i>Sus scrofa</i>	k213	10	14-5258-01	C3B



Product		Code	Size	Art. No.	Barcode
Foods					
rAct d 8 PR-10, Kiwi	<i>Actinidia deliciosa</i>	f430	10	14-4984-01	CG7
rAna o 3 Cashew nut	<i>Anacardium occidentale</i>	f443	10	14-5760-01	D0W
rApi g 1.01 PR-10, Celery	<i>Apium graveolens</i>	f417	10	14-4957-01	CBR
rAra h 1 Peanut	<i>Arachis hypogaea</i>	f422	10	14-4963-01	CDF
rAra h 2 Peanut	<i>Arachis hypogaea</i>	f423	10	14-4964-01	CDG
rAra h 3 Peanut	<i>Arachis hypogaea</i>	f424	10	14-4965-01	CDH
rAra h 8 PR-10, Peanut	<i>Arachis hypogaea</i>	f352	10	14-5341-01	CEZ
rAra h 9 LTP, Peanut	<i>Arachis hypogaea</i>	f427	10	14-4980-01	CFC
rBer e 1 Brazil nut	<i>Bertholletia excelsa</i>	f354	10	14-5343-01	CDS
nBos d 4 alpha-lactalbumin, Milk	<i>Bos spp.</i>	f76	10	14-4522-01	CTP
nBos d 5 beta-lactoglobulin, Milk	<i>Bos spp.</i>	f77	10	14-4523-01	CTR
nBos d 8 Casein, Milk	<i>Bos spp.</i>	f78	10	14-4524-01	CTS
nBos d Lactoferrin, Milk	<i>Bos spp.</i>	f334	10	14-5253-01	C16
rCor a 1 PR-10, Hazel nut	<i>Corylus avellana</i>	f428	10	14-4981-01	CFB
rCor a 8 LTP, Hazel nut	<i>Corylus avellana</i>	f425	10	14-4968-01	CDP
nCor a 9, Hazel nut	<i>Corylus avellana</i>	f440	10	14-5758-01	D0M
rCor a 14, Hazel nut	<i>Corylus avellana</i>	f439	10	14-5754-01	CZP
rCyp c 1 Carp	<i>Cyprinus carpio</i>	f355	10	14-5344-01	CF0
rGad c 1 Cod	<i>Gadus morhua</i>	f426	10	14-4971-01	CEY
nGal d 1 Ovomucoid, Egg	<i>Gallus spp.</i>	f233	10	14-4805-01	904
nGal d 2 Ovalbumin, Egg	<i>Gallus spp.</i>	f232	10	14-4804-01	903
nGal d 3 Conalbumin, Egg	<i>Gallus spp.</i>	f323	10	14-5222-01	C18
rGly m 4 PR-10, Soy	<i>Glycine max</i>	f353	10	14-5340-01	CDR
nGly m 5 beta-conglycinin, Soy	<i>Glycine max</i>	f431	10	14-4990-1	CLV
nGly m 6 Glycinin	<i>Glycine max</i>	f432	10	14-4991-01	CLU
rJug r 1 Walnut	<i>Juglans regia</i>	f441	10	14-5762-01	D0T
rJug r 3 LTP, Walnut	<i>Juglans regia</i>	f442	10	14-5954-01	D11
rMal d 1 PR-10, Apple	<i>Malus domestica</i>	f434	10	14-5703-01	CWR
rMal d 3 LTP, Apple	<i>Malus domestica</i>	f435	10	14-5704-01	CWS
rPen a 1 Tropomyosin, Shrimp	<i>Penaeus aztecus</i>	f351	10	14-5335-01	C11
rPru p 1 PR-10, Peach	<i>Prunus persica</i>	f419	10	14-4960-01	CBV
rPru p 3 LTP, Peach	<i>Prunus persica</i>	f420	10	14-4961-01	CBW
rPru p 4 Profilin, Peach	<i>Prunus persica</i>	d421	10	14-4962-01	CBX
rTri a 14 LTP, Wheat	<i>Triticum aestivum</i>	f433	10	14-5701-01	CN6
rTri a 19 Omega-5 Gliadin, Wheat	<i>Triticum spp.</i>	f416	10	14-4954-01	C8H
Gliadin		f98	10	14-5752-01	CXG
Miscellaneous					
MUXF3 CCD, Bromelain		214	10	14-5339-01	CJU

Educational resources

- Website: **AllergyEducation.co.uk** – Thermo Fisher Scientific educational website explaining the basics of Molecular Allergy and an interactive tool to help with identification of relevant components and interpretation
- Website: **AllergyEducation-MA.com** – Thermo Fisher Scientific educational training course exploring the basics of Molecular Allergy
- Canonica GW, *et al.* A WAO – ARIA – GA2LEN consensus document on molecular-based allergy diagnostics. *World Allergy Organ J* 2013;6(1):17.
- Thermo Fisher Scientific – Cross reactivity in plant food allergy – A focused book on cross-sensitisation
- Thermo Fisher Scientific – Native and cross-reactive allergen components – A more detailed book giving an overview of allergen components
- Thermo Fisher Scientific – Individual literature packs on various components are available. Educational PowerPoint slide sets are also available. Please contact Thermo Fisher Scientific if you would like a set:

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|---------|------------|----------|
| – Egg | – Milk | – Birch |
| – Grass | – Hazelnut | – Peanut |
| – Wheat | – Soybean | – Venoms |
| – Apple | – Walnut | – Cashew |




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