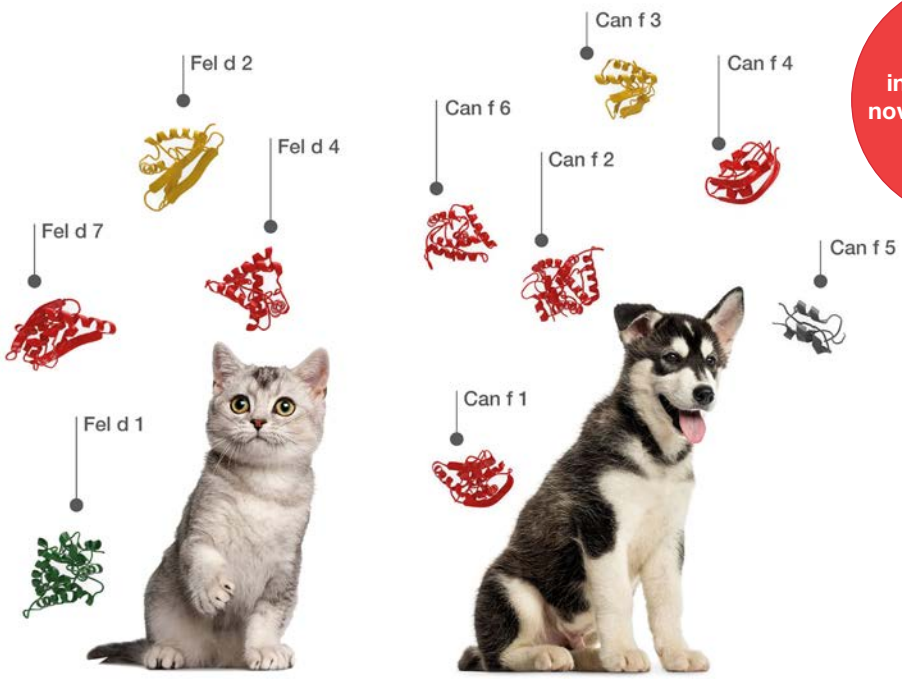

2021 edition with information on novel components rSes i 1 and rPru p 7

Go molecular!

A clinical reference guide to molecular allergy

Part 1: The basics

Revised and updated 2nd edition (2021)

ThermoFisher SCIENTIFIC

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 physicians have commented to me that they could do with a simplified 'all in one guide' so I have tried to simplify molecular allergology based on the allergen components Thermo Fisher Scientific is supplying (manufacturer is Phadia AB).

The intention of part 1 in this guidebook series is to give a basic introduction to molecular allergology 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 allergology, especially protein families, their clinical relevance and nomenclature. If there is one important aspect to learn in molecular allergology it is the scientific relevance of protein families, as they are the key to understanding clinical molecular allergology.

A straightforward summary of the main allergen components, what ImmunoCAP™ products are available and an aid to interpret test results can be found in part 2 of this series – 'The Allergen Components'.

I hope you find this guidebook series useful.

Neal Bradshaw
Portfolio Manager - Allergy
Author of the Go Molecular! books
Immunodiagnostics
Thermo Fisher Scientific

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Contents

Foreword

With the advent of allergen components, allergy has got much more complicated. However whole allergen diagnostics, with skin prick testing or serum specific IgE, commonly don't allow us to unravel the complexity that some of our allergy patients exhibit. Using allergen components to understand the molecular allergology of these complex patients has a real potential to improve our clinical decision-making. The use of component resolved diagnostics may optimize our investigation plans and improve our diagnoses, management plans and the advice we give to our allergy patients. All this though relies on clinicians acquiring an understanding of molecular diagnostics. This is a rapidly evolving area with, for example, the whole peanut allergen suddenly been replaced by more than 10 individual components with different clinical impacts.

This edition of this book is very welcome with its updated information about each of the various allergen components. Importantly, their clinical implications are explained allowing us to use information about allergic sensitization to each individual component to improve the management of our patients.

Professor Graham Roberts
Professor of Paediatric Allergy and Respiratory Medicine
University of Southampton

Introduction: Molecular allergology tells us more

The diagnosis of IgE mediated allergies is made by the physician based on clinical history for the individual patient in conjunction with clinical findings and test results, e.g. specific IgE sensitization tests such as skin prick and/or blood tests and sometimes allergen provocations. Until recently the sensitization tests in use were based on extracts of allergen sources, but in the past years the use of component resolved diagnosis has become increasingly common in clinical practice. Molecular allergology brings a new level of understanding to physicians who seek to improve on existing diagnostic technologies[1-3].

While traditional extract-based IgE blood tests measure the “sum” of sensitization to all protein components in whole allergens, e.g. peanut, molecular allergology makes it possible to investigate important individual proteins within a peanut for specific IgE sensitization. IgE antibody profiles to these molecules vary significantly from patient to patient and they also differ geographically, due to local differences of exposure[1-3].

Molecular diagnostics reveals more factual information about what a patient is allergic to, as individual proteins and profiles can indicate different clinical characteristics[1-3].

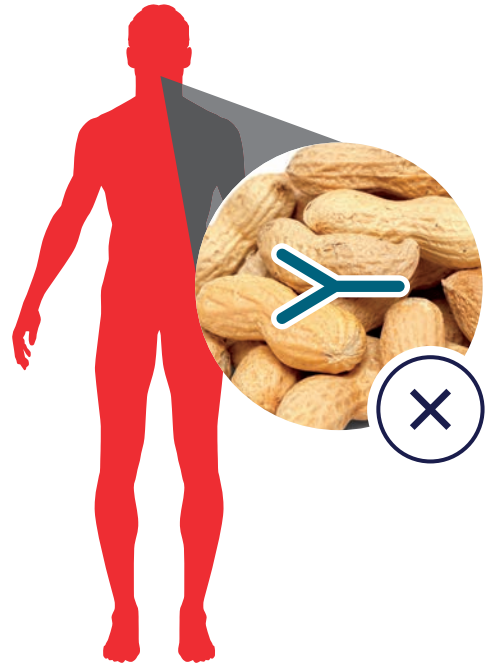
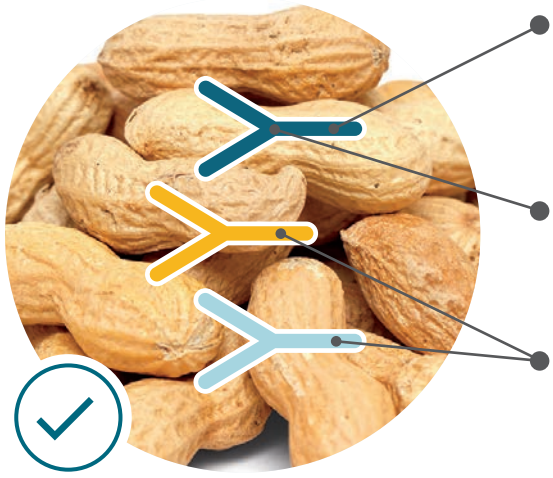


Figure 1: Illustration of the common misconception that there is one IgE antibody produced by the human body for a whole peanut allergen.



The IgE indicated in yellow is directed against peanut Ara h 2*. This can be measured using ImmunoCAP Allergen Components.

Ara h 2 is the most allergenic protein in peanuts. Patients positive to it are at high risk of systemic reactions[1-3]

Other specific IgE antibodies are directed against lower risk peanut proteins such as Ara h 8 and Ara h 5. Proteins closely related to these are also found in tree and grass pollen.

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

Ara h 2/Ara h 6 are the proteins that seems to have the highest allergenic potential of all proteins in peanut. Antibodies produced by patients in response to specific allergen proteins can be measured using single or multiplex allergen component tests, indicating the patients' immunological response in their current allergy status. High levels of IgE to Ara h 2/Ara h 6 will often indicate a patient at high risk of systemic symptoms if peanuts are eaten[1-3].

*ImmunoCAP Allergen f423, Allergen component rAra h 2 Peanut

Clinical relevance

Allergen component diagnostics measures IgE to specific 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 for allergic reactions – adding confidence to your assessment[1-3].
2. Aiding the selection of the proper treatment extract of Allergen Specific Immunotherapy (AIT) – useful for example in venom and aero-allergy patient selection[1-3].
3. Understanding cross-reactions between species – helping to understand multiple sensitizations e.g. in pollen food syndrome[1-3].

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

Much of the clinical value of testing with allergen components up to now has been demonstrated within food allergy, especially with plant foods such as nuts, fruits and legume seeds. The majority of information in this reference guide therefore focuses on food allergen components, although an overview of other allergen components which provide clinical value, such as those in pollen, furry animals, mites, latex and insect venoms, is also included.

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Protein families

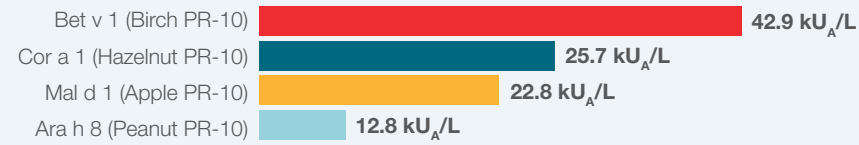
Introducing testing with molecular allergens into daily clinical practice will help improve diagnosis of allergy based on allergenic proteins and protein families.

Protein families referred to in this guide are families with similar functions and structures found in many allergen sources[1-8]. For example, plant seeds contain storage proteins such as vicilins, transport proteins such as lipid transfer proteins and defense proteins such as PR-10s (pathogenesis-related family number 10 proteins). Lipocalins and serum albumins are examples of protein families found in mammalian allergen sources[1-8].

Below is an example showing the IgE test results of a patient with suspect plant food allergy.

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

IgE test results of a patient with suspect plant food allergy



- Traditional thinking: four different specific IgE reactions to four different plant sources.
- On the 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 sensitized to other PR-10 proteins not measured. From the above extrapolations can be made of other PR-10 sensitization 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 for example be applied to profilin or nsLTP (lipid transfer protein) profiles (if positive).

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 specific IgE. The presence of allergen-specific IgE usually indicates a risk of allergy symptoms and **a result** of **≥0.1 kU_A/L indicates sensitization**. Some molecular allergens are associated with a higher risk for systemic reactions, while others are considered to pose no or a very low probability for severe reactions. A high IgE-level to an allergen such as Ara h 2 or Cor a 14 often means a high risk of symptomatic allergy[1-3].

However for different patients identical results for the same allergens may not be associated with clinically equivalent manifestations, due to differences in individual patient sensitivities. This may also be true for one individual patient at different occasions due to presence or absence of reaction promoting cofactors [1-3].

Always consider test results in association with a clinical history.

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Allergen component nomenclature

The WHO/IUIS Committee

Allergen and allergen components are identified and categorized 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[1]. For further information check the IUIS allergen nomenclature website at: **allergen.org**.

Allergen components are given a name based on an abbreviation of 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)[1]. An example of peanut allergen component nomenclature:

Peanut – ***Ara****chis* ***h****ypogaea* – Ara h 2

Thermo Fisher Scientific, the leading supplier (Phadia AB is the 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 WHO IUIS recognized allergens at **allergen.org**.

References

1. Radauer C et.al. Update of the WHO/IUIS Allergen Nomenclature Database based on analysis of allergen sequences. Allergy 2014; 69: 413–419.

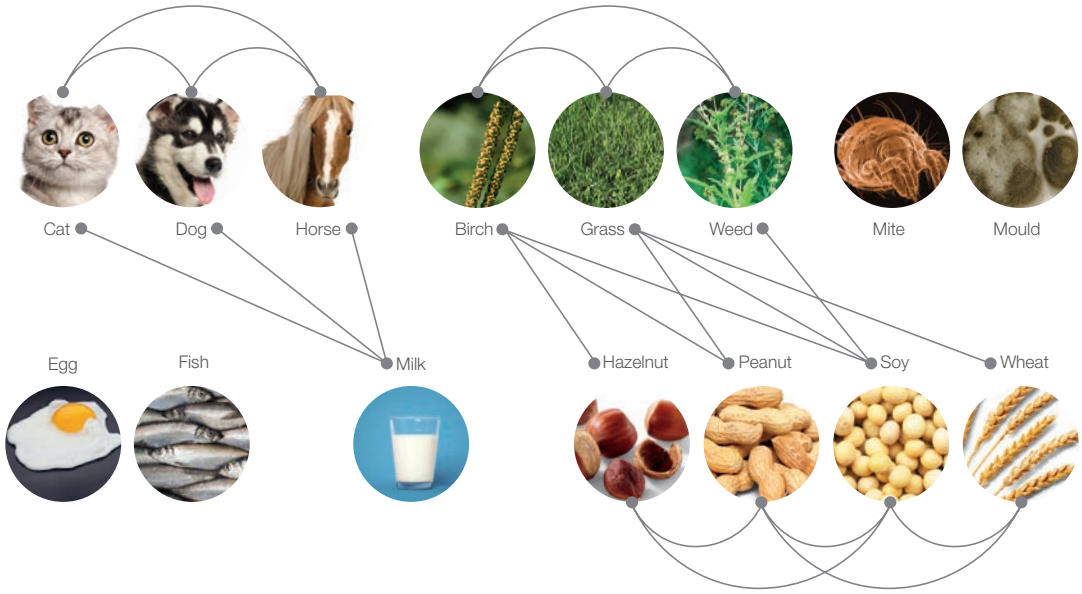
Specific and cross-reactive allergens

Molecular allergens can be split into allergens with high and low potential for triggering clinical symptoms. These allergens can then also be further grouped into molecules specific to an allergen source and molecules with great similarities even between distantly related allergen sources. Such allergens are said to be cross-reactive. Differentiating between sensitization to specific and cross-reactive allergen components helps us to better understand the characteristics of an individual's allergy profile[1-3].

The below figure demonstrates a typical allergen test panel. Many of the allergens could give rise to IgE cross-reactions.

For instance, dog, cat and horse all contain members of the lipocalin protein family together with serum albumin which is also found in milk. Birch, grass and weeds contain profilins, which are found in legumes such as soy and peanut, as well as in wheat and hazelnut. IgE cross-reactions can confound extract based test results, which makes it difficult to understand what the primary allergen causing the symptoms is. ImmunoCAP Allergen Component tests and the multiplex ImmunoCAP ISAC help to improve diagnostic clarity[1-3].

Figure 3: Illustration of a typical allergen test profile



You can learn more about the significance of these types of allergens at: **allergyai.com**.

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

References

1. Matricardi PM et al. EAACI Molecular Allergology User's Guide. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology. 2016;27 Suppl 23:1-250.
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Other clinical considerations

Allergen load

The patient's clinical history remains the most important part of allergy diagnosis. Component testing will reveal crucial information but as with any IgE test it should be used in support of the clinical history. Only the clinical history can reveal how much of each food allergen the patient has ingested. For example, when consuming large amounts of allergens at the same time, such as when drinking a soy milk drink can affect the symptom outcome[1-3].

Low risk allergens such as PR-10 proteins found in soy milk, when consumed in great amounts can provoke more serious allergy symptoms in some patients (such as drinking soy milk[1-2]).

A patient sensitized to several allergen sources will often be sensitized to several allergen components. This will contribute to the overall allergen load. For example, if a patient is positive to multiple peanut storage components such as Ara h 1, Ara h 2 and Ara h 3, he or she is likely to have a higher IgE load and therefore possibly be at more risk for severe reactions than someone who is mono-sensitized[1-5].

Diagnostic performance

Extract-based tests (whole allergens) contain a mix of many different proteins from an allergen source (e.g. peanut) and measure the sum of IgE antibodies to these, which gives high sensitivity, but sometimes can create difficulties in interpretation of results[1-5].

ImmunoCAP Allergen Component-based tests, both singleplex and multiplex, contain pure proteins, measure only specific IgE to single molecules and give results with high diagnostic specificity[1-5].

Allergen component tests therefore have technical diagnostic superiority at measuring IgE to important individual proteins of interest, such as to Ara h 2 in peanut or Cor a 14 in hazelnut. They simply measure IgE specific to one protein and offer reliable results in terms of minimal variation – like all ImmunoCAP products. However, it must be remembered that a test with allergen components only measures one type of specific IgE and that most patients will have IgE antibodies to several molecules contained in the allergen source[1-5].

Presence of allergen specific IgE implies a risk of allergic disease and its significance must be evaluated within the clinical context. Generally the higher the level of IgE antibodies the higher the probability of a clinically manifest allergic reaction[1-5].

However, for different patients identical results for the same allergens may not be associated with clinically equivalent manifestations, due to differences in individual patient sensitivities. This may also be true for one individual patient at different occasions due to presence or absence of reaction promoting cofactors[1-5].

Absence of detectable allergen specific IgE antibodies does not necessarily exclude the potential for an allergy-like reaction[1-2].

For example in food allergy, circulating IgE antibodies may remain undetectable despite a convincing clinical history. The antibodies may be directed towards allergens that are revealed or altered during industrial processing, cooking or digestion and therefore do not exist in the original food for which the patient is tested[1-2].

Limitations of ImmunoCAP products test results:

Samples with results below limit of quantitation obtained with ImmunoCAP Allergen Components are recommended to be tested with the corresponding extract based ImmunoCAP Allergen and/or additional relevant ImmunoCAP Allergen Components, if not already performed and a clinical indication is present. The extract based testing can cover additional allergen components present in the allergen source material to which the patient may be sensitized, but which are not presently available as ImmunoCAP Allergen Components or in ImmunoCAP ISAC.

A result below limit of quantitation obtained with an extract based ImmunoCAP Allergen never excludes the possibility of obtaining measurable concentrations of specific IgE when testing with ImmunoCAP Allergen Components from the same allergen source. This is due to the fact that some components may be present in very low amounts in the natural extract.

In most cases it is recommended that testing starts with whole allergens to achieve high sensitivity to be followed up with allergen component tests for further specificity and as an aid in risk assessment if the test for the whole allergen is positive[1-5].

Further information at **allergyai.com**.

References

1. Matricardi PM et al. EAACI Molecular Allergology User's Guide. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology. 2016;27 Suppl 23:1-250.
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Food allergy

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. liquidizing or concentrating (as for fruit juices)[1-2].

There are many different metabolic processes that occur as soon as food enters the digestive system. Enzymatic digestion starts straight away in the mouth; acidic pH and gastric juices play a role as food enters the stomach and further digestion takes place in the gut until the food is absorbed as smaller nutrients[1-2].

Fats are metabolized into fatty acids; carbohydrates are eventually broken down into small sugar molecules, while proteins are digested into their constituents - amino acids. Most allergens are proteins, made up of amino acid chains, and within these structures are regions called epitopes. It is these recognition sites that specific IgE molecules bind to. This can lead to the release of histamine and other mediators, resulting in allergy symptoms[1-2].

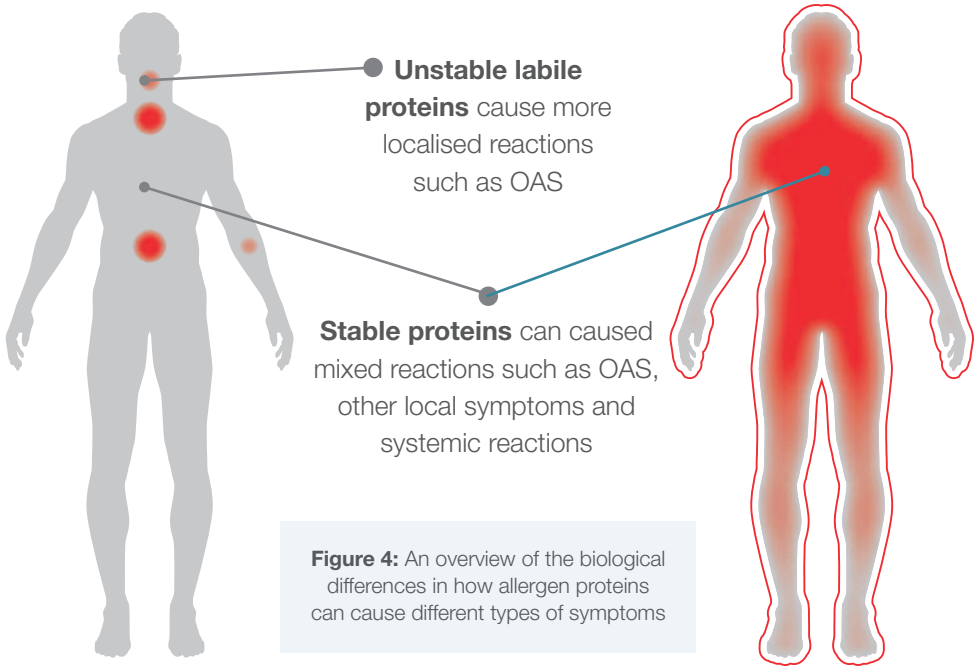

Figure 4: An overview of the biological differences in how allergen proteins can cause different types of symptoms

Molecules of high allergenic potential

Some proteins are more resistant than others to metabolic processes, due to their robust chemical structures; e.g. storage proteins from peanut (Ara h 1, Ara h 2, Ara h 3 and Ara h 6) or ovomucoid from hen's egg (Gal d 1). As these allergens have higher resistance to digestion, their allergenic potential is also higher as their epitope structures stay intact longer. As a result, these proteins cause more systemic symptoms than unstable proteins (figure 4)[1-10].

Molecules of low allergenic potential

Certain allergen molecules such as PR-10s and profilins (present in nuts, fruits and pollen) are more labile in structure and therefore susceptible to digestive processes such as heating/cooking and enzyme activity in the gastrointestinal tract. Such labile proteins start to break down already in the mouth, causing less problematic reactions such as oral allergy syndrome (OAS). As the epitope binding regions in these proteins are destroyed, these molecules tend not to induce systemic symptoms[1-10].

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 sensitized 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 proteins a patient is IgE positive to unless they were separated individually – as they are when using ImmunoCAP Allergen Component tests. Also, all patients vary in which components they are sensitized to[1-10].

ImmunoCAP offers a large portfolio of different allergen components, enabling the mapping of individual patient profiles and improving diagnostic clarity. ImmunoCAP ISAC is a multiplexing test that measures IgE to a total of 112 allergen components and through cross-reactivity one can extrapolate sensitizations to other clinically relevant allergen sources[6].

Patients testing positive to a whole extract (e.g. positive skin prick test to peanut or serum IgE to peanut) can be sensitized to either allergen proteins of high allergenic potential or of low/no allergenic potential. By using molecular diagnostics it is possible to better differentiate between them, i.e. classify patients into low- and high-risk groups. There are of course also cases where the patient is sensitized to both high-risk and low-risk allergens and can display symptoms such as OAS together with systemic symptoms[1-10].

Furthermore, in a given situation other factors such as amount of allergen, stress, ongoing infections etc have an impact on the actual clinical reaction[1-2].

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 mostly food proteins more resistant to digestion. Such primary sensitization to stable proteins is therefore often associated with systemic allergy symptoms[1-10.]

Cross-reactive sensitization and pollen-food syndrome

Allergen components that have highly similar structures in several different species can give rise to extensive cross-reactivity, these are referred to as “pan-allergens”. Pan-allergens are commonly found in plants and plant derived foods and they can be found even in distantly related species such as celery and birch trees[1-10].

Sensitization to pan-allergens may be both asymptomatic and symptomatic, but the symptoms elicited are often of a milder form, such as OAS. In pollen-allergic patients for instance, IgE antibodies primarily targeted towards proteins in pollen (e.g. birch Bet v 1) readily cross-react with similar proteins in food, causing a broad sensitization profile which can be considered “secondary” to the pollen sensitization. In clinical allergy, this is often referred to as pollen-food syndrome and in the context of latex, the latex-fruit syndrome[1-10].

Cross-reactive allergens exist also in other sources, such as venoms of stinging insects, fish, mites and shrimp. For example, dust

mite and shrimp share a cross-reactive protein called tropomyosin[1-5].

When sensitization to cross-reactive allergens is detected, the primary sensitizer should always be sought after in order to understand what is driving the patients' allergy. Using a range of specific and cross-reactive allergen component tests it is in most cases possible to differentiate primary and secondary reactions[1-10].

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Plant components

Plant protein 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 e.g. pollen allergen epitopes to bind to similar allergen epitopes in food. This immunological mechanism is often the cause for broad sensitization patterns seen in many allergic patients. The dominant sensitizing plant aeroallergens in Northern Europe are pollen from birch and temperate grass species such as Timothy grass, while in Southern Europe olive and grass pollen are the main culprits of hay fever symptoms. Patients with hay fever may often experience local symptoms from certain plant-derived foods, due to cross-reactive proteins common to different plants[1-10].

Plant proteins involved in allergy include storage proteins, LTPs, PR-10s and profilins. Another type of molecular structure to take into account is CCDs (cross-reactive carbohydrate determinants). Further references regarding plant food proteins can be found towards the end of this section[1-10].

Storage proteins

Storage proteins are biological reserves of amino acids used by plants to grow, found in e.g. legumes, seeds and nuts. 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 2S albumins (e.g. Ara h 2 and Ara h 6 in peanut and Ber e 1 in Brazil nut) are some of the most stable plant food molecules and therefore the most clinically important. The 2S Albumins such as Ara h 2 molecules are not easily destroyed by gastric fluids 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)[1-5].

LTPs (Lipid Transfer Proteins)

LTPs are very stable small molecules widespread in plant food such as fruits and nuts. They are found concentrated in the skin of *Rosaceae* fruits, especially in the peel of peach – the pulp contains less of the allergen. LTPs from different species can be highly cross-reactive. IgE sensitization to LTPs has mostly been 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 connection with nuts such as walnut and hazelnut and in peanut[1-5, 8].

The LTP sensitization pattern in Northern Europe is not completely understood and not as well documented as in Southern Europe, where LTP sensitization is very common. The protein characteristics of LTPs explain their

clinical relevance due to their high resistance to heat and protease digestion. However, LTP sensitization is also associated with local reactions including OAS[1-5, 8].

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

The plant defense proteins of the PR-10 family are present in pollen of *Fagales* tree species (e.g. birch, hazel, alder and beech) and can also be found in the pulp of fruit. Bet v 1 is the major allergen in birch pollen and is highly similar to other PR-10 proteins in plant foods such as *Rosaceae* fruits (peach, apple and cherry etc.), as well as to PR-10s in nuts and legumes.

In a typical birch allergy scenario, birch pollen causes a primary sensitization 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 ingest 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)[1-5, 9].

Profilin proteins

Profilin proteins occur in many different plant species and cause broad sensitization patterns. They are found for example in pollen (e.g. birch or grass), fruit (e.g. apple, cherry, melon and banana) and vegetables, nuts and latex. It has been proposed that just one profilin from one plant species is enough for testing IgE sensitization to profilin, due to the close similarity and extensive 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 sensitization may cause severe reactions[1-5, 10].

CCDs (Cross-reactive Carbohydrate Determinants)

Some molecular structures such as CCDs are shared between many species and can be found in insect venoms, pollen and plant foods. CCDs are not proteins but specific parts of carbohydrate chains attached to proteins. The clinical impact of specific IgE to CCDs is considered very low although positive IgE test results are frequent[1-7].

CCDs help us to understand poly-sensitization to multiple plant foods and latex or double positivity between bee and wasp venoms. It is also worth noting that natural plant allergen extract preparations contain CCD molecules while recombinant sources typically are CCD-free and hence more specific[1-7].

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Interpreting results from cross-reactive protein families

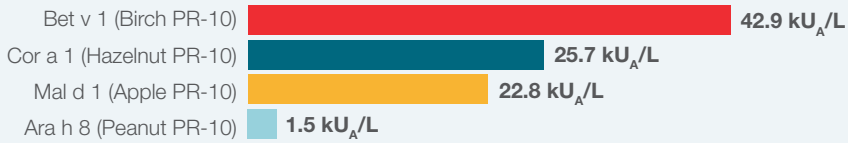
Example 1

A variety of allergen component tests could be used when resolving a patient's birch-food allergy. Is it a primary food allergy? Bet v 1 is a dominating primary sensitizing allergen in a birch allergic patient and could produce cross-reactions between other plant food species.

The example below demonstrates a patient profile of PR-10 sensitization with a suspected case of IgE-mediated peanut allergy. In this example, all other risk allergens such as Ara h 2 in peanut or Cor a 14 from hazelnut were IgE-negative.

Like all ImmunoCAP Specific IgE tests, ImmunoCAP Allergen Components give results in kU_A/L (ImmunoCAP ISAC gives semi-quantitative results in ISU-E). Primary sensitizing allergens from within the same protein family (in this example PR-10) will normally give the highest specific IgE level. Other secondary IgE sensitizations will give similar specific IgE readings but normally lower levels than the primary sensitizing allergen due to reduced protein homology (and therefore reduced IgE binding)[1-6].

Example 1: PR-10 sensitization with a suspected case of IgE-mediated peanut allergy



Clinical interpretation:

- Food-pollen syndrome caused by a primary PR-10 birch-pollen allergy
- Likely symptoms local/mild or none e.g. oral allergy to hazelnut, apple 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 has a primary sensitization to an allergen component that does not cross-react (such as a storage protein) then this serves as a diagnostic marker of risk for severe reactions which is covered further in this guide[1-6].

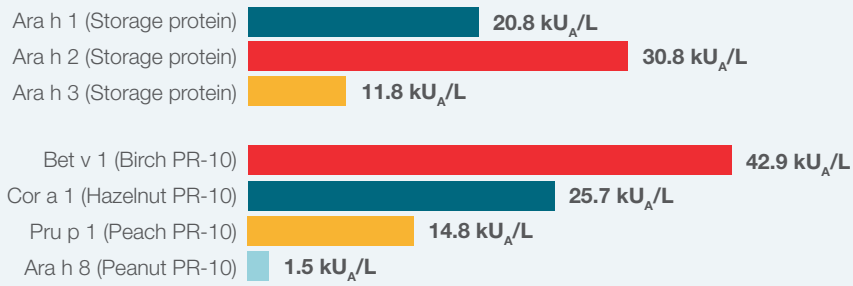
Example 2

Using the example of suspected peanut allergy (see figure Example 2 below) the IgE results could be interpreted like this:

Clinical interpretation:

- Primary sensitization 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 higher risk of severe, systemic symptoms
- The patient also has concomitant birch sensitization 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 e.g. oral allergy, or none
- Both systemic and local symptoms might occur

Example 2:



Always use the test results in combination with a clinical history. The presence of specific IgE is not always associated with clinical symptoms but represents a risk of allergic reactions on allergen exposure.

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Summary of plant food components

Plant protein families are common to many species and the closer the species are related the more similar the proteins can be. But also in distantly related species there are proteins that are very similar which can give rise to cross-reactivity. Thus, IgE molecules directed against pollen allergen epitopes can bind to similar allergen epitopes in foods such as peanuts, tree nuts, fruits and vegetables[1-5].

The majority of food allergen components in plants belong to four main protein groups. These are storage proteins, LTP, PR-10 and profilin proteins. In addition, CCDs (Cross-reactive Carbohydrate Determinants) are allergenic structures found in pollen and plant food, as well as in insects and venoms[1-5].

Protein family	Risk for systemic reactions?	Do I have to consider many different allergen sources?
● **Storage proteins**	**High.** 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).
● **LTP**	**Moderate to High.** LTPs 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 LTPs 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.** 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).

Table References

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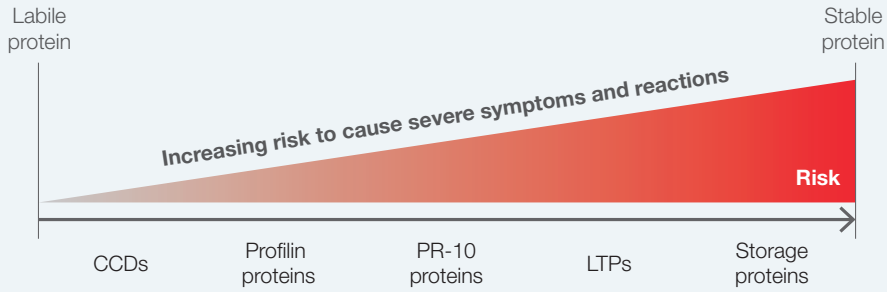
Figure 5:



An overview of the biological differences in how allergen proteins can cause different types of symptoms

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Plant allergen components in some common foods

Allergen source/ Component family	Profilin	PR-10	LTP	Storage proteins: 2S Albumin	Storage proteins: Vicilin-like 7S globulin	Storage proteins: Legumin-like 11 S globulin	Other
Peanut	Ara h 5	**Arah 8**	**Ara h 9,** 16, 17	**Ara h 2, 6,** 7	**Ara h 1**	**Ara h 3**	Ara h 10-15
Soy	Gly m 3	**Gly m 4**		Gly m 8	**Gly m 5**	**Gly m 6**	Gly m 7
Hazelnut	Cor a 2	**Cor a 1**	**Cor a 8**	**Cor a 14**	Cor a 11	**Cor a 9**	
Walnut	Jug r 7	Jug r 5	**Jug r 3,** 8	**Jug r 1**	Jug r 2, 6	Jug r 4	
Pecan				Car i 1	Car i 2	Car i 4	
Cashew				**Ana o 3**	Ana o 1	**Ana o 2**	
Pistachio				Pls v 1	Pls v 3	Pls v 2, 5	Pls v 4
Brazil nut				**Ber e 1**		Ber e 2	
Sesame				**Ses i 1** / Ses i 2	Ses i 3	Ses i 6, 7	Ses i 4, 5
Sunflower seed	Hel a 2		Hel a 3	*Hel a 2S Albumin*			
Rape seed	*Bra n 8*			Bra n 1			*Bra n 4, 7*
Cabbage	*Bra o 8*		Bra o 3				
Mustard	Sin a 4		Sin a 3	Sin a 1		Sin a 2	
Buckwheat				**Fag e 2**	Fag e 3		Fag e 4
Kiwi	Act d 9	**Act d 8,** 11	Act d 10	Act d 13		Act d 12	**Act d 1, 2, 5**
Melon	Cuc m 2	Cuc m 3					Cuc m 1
Tomato	Sola l 1	Sola l 4	Sola l 3, 6, 7				Sola l 2, 5
Apple	Mal d 4	**Mal d 1**	**Mal d 3**				Mal d 2
Pear	Pyr c 4	Pyr c 1	Pyr c 3				Pyr c 5
Almond	Pru du 4	Pru du 1	Pru du 3			Pru du 6	Pru du 5
Peach	**Pru p 4**	**Pru p 1**	**Pru p 3**				Pru p 2 / **Pru p 7**
Apricot		Pru ar 1	Pru ar 3				
Plum	*Pru d 4*	*Pru d 1*	Pru d 3				Pru d 2, 7
Cherry	Pru av 4	Pru av 1	Pru av 3				Pru av 2

Bold Available as single ImmunoCAP Allergen Component

Bold Available on ImmunoCAP ISAC$_{112i}$ Chip only

Normal WHO/IUIS listed

Italic Described in peer reviewed literature

Likely but not yet described

Allergen source/ Component family	Profilin	PR-10	LTP	2S Albumin	Vicilin-like 7S globulin	Legumin-like 11 S globulin	Other
			Storage proteins				
Strawberry	Fra a 4	Fra a 1	Fra a 3				
Raspberry		Rub i 1	Rub i 3				
Carrot	Dau c 4	Dau c 1	*Dau c 3*				Dau c 5
Celery	Api g 4	**Api g 1**	Api g 2, 6				Api g 3, 5
Wheat	Tri a 12		**Tri a 14**				**Tri a 19, Gliadin,** many more
Barley	Hor v 12						Hor v 15-17, 20
Rice	Ory s 12						
Maize	Zea m 12		Zea m 14				Zea m 8
Plants often driving sensitization							
Birch	**Bet v 2**	**Bet v 1**					
Timothy	**Phl p 12**						
Latex	**Hev b 8**		Hev b 12				**Hev b 5, 6, 11**

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www.allergen.org and www.allergome.org

Other allergen components

Allergen Component testing also provides useful information about other allergen sources such as non-plant foods, furry animals, mites, molds, pollen and venoms from stinging insects. Below is a brief overview, although further information on clinical interpretation and what ImmunoCAP Allergen 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 references below for each allergen section.

Egg and milk

Foods such as milk and egg are associated more with pediatric allergy, and children tend to outgrow these allergies at a young age[1-7]. However, in a recent longitudinal egg allergy study in the UK it was shown that many children don't outgrow their egg allergy until well past 5 years of age, in fact the median age in this study was 10 years for egg allergy resolution[5].

Egg and milk contain allergen components that are markers for reactivity to different forms of allergy. The allergenicity of hen's egg Gal d 1 (Ovomucoid) and cow's milk Bos d 8 (Casein) is not destroyed by heating, and patients negative to Gal d 1 and/or Bos d 8 IgE tests have been observed to tolerate cooked forms of egg and milk[1-7]. Allergy persistency is associated with IgE to the same allergens, and therefore IgE to Gal d 1 and Bos d 8 can be used as markers of clinical reactions and tolerance development to egg and milk, respectively[1,2,5-7].

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Red meat

Recently a previously unrecognized clinical syndrome has been reported where systemic reactions occur several hours after the ingestion of mammalian meat (beef, pork, lamb and offal, e.g. kidney)[1-8]. Most cases have concerned adults, but recent reports also include children[6]. Whereas food allergy symptoms generally occur shortly after ingestion, this type of red meat allergy is associated with symptoms delayed 3-6 hours. The most common symptoms include gastrointestinal problems, urticaria and anaphylaxis[1-8].

A carbohydrate, the oligosaccharide

Galactose-alpha-1, 3-Galactose (alpha-gal), appears to be the allergen causing the reactions[1-8]. Alpha-gal is present in many mammalian proteins including beef, pork and lamb[1-2,5]. The primary hypothesis in the attempts to explain the causes of IgE antibody responses to alpha-gal is that previous tick bites may be a causative factor[1-2,7,8]. Measuring specific IgE to alpha-gal is a tool that can be used to support the diagnosis of this type of red meat allergy and also sensitization to the cancer drug cetuximiab which contains the alpha gal epitope[1-9].

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Shellfish and crustaceans

Shellfish and particularly prawns make up one of the major allergenic food groups[1-5]. Tropomyosin (Pen a 1, Pen m 1) is considered a major allergen in shrimp and crustacean allergy[1-6]. Tropomyosin proteins are highly cross-reactive actin-binding proteins located in muscle fibers amongst many invertebrate species such as shrimps (Pen a 1), and other crustacean foods such as crab, lobster and molluscs as well as dust mites (Der p 10) and cockroaches (Bla g 7). Due to its wide-spread occurrence, tropomyosin can be both inhaled and ingested. About 10% of dust mite-allergic patients have IgE to tropomyosin. Some studies suggested that dust mite immunotherapy or respiratory exposure to dust mite tropomyosin may induce tropomyosin sensitization causing food allergy to shrimps[1-3].

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Fish

Parvalbumins such as Gad c 1 (cod, white fish) and Cyp c 1 (carp) are major fish allergen components and markers of fish sensitization[1-6]. Fish-allergic patients can sometimes tolerate certain fish species while reacting to others. However, as parvalbumins from different fish species are structurally closely related and highly cross-reactive, analysis of IgE antibody binding to them is generally not informative in regard to discriminating between allergies to different species of fish. A positive test result to either of Gad c 1 and Cyp c 1 nevertheless indicates a risk of severe reactions to fish[1-6]. Parvalbumins are expressed in lower amounts in certain fish species such as tuna, swordfish and some mackerels. This perhaps explains why some fish-allergic patients can tolerate these species[4-6].

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Furry Animals

Furry animals such as dogs, cats and horses produce some of the most prevalent allergens in our environment and are released into the surroundings through animal saliva, dander and urine. Like many other allergen sources furry animals contain both specific and cross-reactive allergen components[1-3].

Clinically uteroglobin and lipocalins have been identified as the most important major allergen components from cat, dog and horse[1-7]. Serum albumins are often considered to have less clinical relevance in allergy to furry animals, they are minor allergens which cause multiple positivity due to cross-reactivity when using extract tests[1-3]. However serum albumins are important food allergens in meat[1-3,8].

Children with problematic severe asthma often have higher levels of IgE antibodies towards cat, dog and horse compared with children with controlled asthma[5-6]. Revealing the primary allergen source driving the allergy could help improve allergy management such as allergen reduction/avoidance strategies, and be an aid to select the proper Allergen Specific Immunotherapy (AIT). AIT success is more likely if sensitization to specific components is identified and appropriate therapy administered[3,9-10].

References

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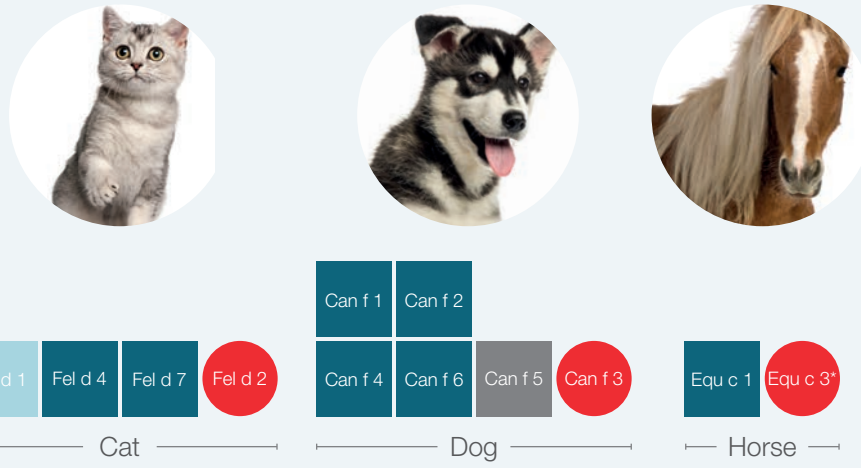
60-70% of pet sensitized patients are sensitized to serveral pet extracts - specific or due to cross-reactivity sensitization[11]

Typical allergens[12]



Specific components in squares

Uteroglobin | Lipocalin family | Kallikrein | Serum albumins

Protein family	Summary	Clinical Importance
Uteroglobin	Uteroglobin, a steroid-inducible cytokine-like molecule with anti-inflammatory and immunomodulatory properties.	**High.** Fel d 1 the major cat allergen belongs to this family.
Lipocalin family	Small, specific molecules. Although highly conserved they display limited sequence identity of between 20 – 30%.	**High.** Lipocalins are often major allergens and constitute an important primary allergen.
Kallikrein	Kallikreins are peptidases. Prostate specific antigen (PSA) is a kallikrein which liquefies semen and allows sperm to swim freely.	**High.** Associated with male dogs (Can f 5). A major allergen.
Serum albumin	Large globular proteins present in dander, saliva, meat and milk.	**High.** Highly cross reactivity, minor allergen and is seldom of clinical importance.

**Available on ImmunoCAP ISAC*

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House dust mites

Allergy to house dust mites (HDM) is a main cause of respiratory allergies in most parts of the world, and exposure to HDM is a major trigger of asthma exacerbations[1-4]. *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farinae* (Der f) are the most common HDM species, both containing the major allergens - group 1 and 2 proteins. The homology between the two mite species is very high and cross-reactions are common[1-3].

Der p 1/Der f 1 and Der p 2 /Der f 2 have for a long time been known to be major mite specific allergens[1-4]. Recently several other mite allergens have been identified and Der p 23 has been recognized as also being a major mite component with high clinical relevance[5-6]. Sensitization to increasing numbers of mite components seem to indicate more severe disease[6].

Tropomyosin (Der p 10) is the main cross-reactive allergen between mites, shellfish, cockroaches and helminths. Tropomyosin is a minor allergen in mite allergy but considered a major allergen in shellfish allergy[1-3].

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Pollen

Grasses

All grasses belong to the same botanical

family, *Poaceae*, therefore cross-reactivity between different species is common and the closer the relations (e.g. within subfamilies), the higher the degree of cross reactivity[1-4]. Grass pollen allergy is common worldwide, and many atopic patients show sensitization to grass pollen[1-6]. Grass pollen season overlaps with weed pollen such as mugwort and ragweed in most parts of Europe and with tree pollen (olive, plane) in Southern Europe [1-3,5]. Group 1 and group 5 allergens (e.g. Phl p 1 and Phl p 5 from Timothy) are dominating grass pollen allergens and markers of primary sensitization in a majority of patients[1-6]. Sensitization to Phl p 1 usually precedes other grass pollen component sensitizations in the development of hay fever symptoms[6]. In warmer areas, other grass species such as Bermuda grass are common and they also contain group 1 allergens e.g. Cyn d 1[1-5]. Sensitization to cross-reactive allergens such as profilin (Phl p 12) and polcalcin (Phl p 7) is usually not frequent but several grass allergens carry CCD which can cause cross reactivity in extract based testing[1-7].

When no specific grass sensitization is detected other pollen or food specific components should be investigated[1-3,5].

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Trees

Opposed to grasses, trees belong to several different botanical families, often even to different orders, and there is less cross-reactivity between specific tree allergens. However all tree pollen contain profilin and most contain polcalcins and CCDs, giving rise to possible cross-reactivity on the extract level[1-8].

Due to Bet v 1 sensitization (the major birch allergen) many birch pollen allergic patients react to several pollen, such as the closely related alder, hazel, beech and oak[1-3,6.] In addition, many of these patients have concomitant pollen-related food allergies due to PR-10 cross-reactivity (Bet v 1) and may react to various fruits, nuts and vegetables (e.g. apple, pear, cherry or hazelnut)[1-3]. In most cases, symptoms are restricted to oral reactions and the food is often tolerated when cooked since PR-10 allergens are heat labile[1-3].

Olive and ash are botanically very closely related (*Oleaceae* family) and there is extensive cross-reactivity between these

species[1-5,7]. Olive tree pollen allergy is quite common and is one of the most important causes of seasonal respiratory allergy in the Mediterranean area[5,7]. Ole e 1 is the major marker for primary olive pollen sensitization[1-5,7]. The European ash *(Fraxinus excelsior)* is common in most of Europe but ash tree pollen may often be overlooked as a cause of pollinosis[1-2,5]. Ole e 1 serves as a very good marker allergen for ash due to the high cross reactivity[1-5,7].

Plane trees are known as “street trees” and are found planted practically anywhere in the world[1-2]. Recombinant Pla a 1 is a specific marker allergen discriminating between genuine plane tree pollen sensitization and cross-reactivity[1-5]. Pla a 3 is a LTP which cross-reacts with other LTPs in e.g. fruits[1-3]. Pla a 3 is presently not available as a single ImmunoCAP Allergen Component. However, Pla a 3, as well as the plane-tree specific and major allergen Pla a 1 are available on the ImmunoCAP ISAC$_{112i}$ Chip.

Cypresses and cedars are common ornamental trees[1-5]. There are several species of cypress and cedars and since they are closely related cross-sensitization is extensive. Cypress trees bloom in the winter and may cause winter respiratory allergy which is often misdiagnosed since symptoms are occurring during winter and are very similar to perennial allergies like dust mite allergy[1-3,8,9]. Cup a 1 is a specific marker for primary sensitization to *Cupressaceae* pollen. The Cup a 1 allergen is very similar to major allergens of Mediterranean cypress (Cup s 1) Mountain cedar (Jun a 1) Japanese cypress Cha o 1) and Japanese cedar (Cry j 1) and there is an extensive cross-reactivity between species[1-4,8,9].

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Weeds

Weed allergy diagnosis can be unclear and difficult to make due to frequent poly-sensitizations and inconclusive anamnesis because of overlapping flowering seasons with other pollen such as birch and grass[1-3]. Cross reactions are expected between different weed species when botanically closely related, however many weeds belong to unrelated botanical families and therefore specific marker allergens are available,

e.g. Amb a 1 from Ragweed, Art v 1 from Mugwort, Par j 1 from Parietaria, Pla l 1 from English plantain and Sal k 1 from Saltwort[1-5]. Saltwort is a weed common in dry, semi-arid areas and is becoming more and more common in southern parts of Europe due to climate change.

Apart from profilin and CCDs, mugwort and ragweed pollen contain some other cross-reactive allergens. Cross-reactive IgE antibodies can lead to clinically significant allergic reactions[5].

Pollen-food syndromes driven by weed pollen are mainly generated by mugwort and ragweed pollen. In addition to Oral Allergy Syndrome (OAS) more severe allergy is reported such as the celery-mugwort-spice syndrome[1-2,6].

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Molds

There is current evidence to demonstrate a close association between fungal sensitization and asthma severity[1-5]. Many airborne fungi are involved such as *Alternaria*, *Aspergillus*, *Cladosporium* and *Penicillium*, and exposure may be indoors, outdoors or both. Fungal sensitization is common in asthmatic patients and the term "severe asthma with fungal sensitization" (SAFS) has been proposed[1-5]. However, it is recognised that enhanced and precise definition of fungal sensitization will require improvements in diagnostic testing and this can be facilitated by component testing[1-9].

Alternaria alternata is a major outdoor as well as indoor aeroallergen in many parts of the world. Sensitivity to *Alternaria* has been increasingly recognized as a risk factor for the development and persistence of asthma, asthma severity, and potentially fatal asthma exacerbations[2-6]. Alt a 1 is the major *Alternaria* allergen. Alt a 1 is considered a specific marker of primary sensitization to *Alternaria Alternata* and useful in asthma diagnostics[2-6].

Aspergillus fumigatus is an opportunistic fungus causing allergic and invasive aspergillosis in humans and animals[1-4,7-9] Genuine *A. fumigatus* sensitization is not always easily identifiable and IgE sensitization tests are used as part of routine workup for diagnosing Allergic Bronchopulmonary Aspergillosis (ABPA). The use of allergen components for *A. fumigatus* can aid the identification of primary *A. fumigatus* sensitization[1-4,7-9].

Asp f 1, Asp f 2 and Asp f 4 are species specific allergens while Asp f 3 and Asp f 6 are described as cross-reactive allergens[1,2,7-9]. Recent studies investigating ABPA demonstrated that ImmunoCAP Allergen Components could differentiate ABPA from asthma and sensitised patients. ABPA has been particularly linked to Asp f 4 and Asp p 6[7-9] – see book 2 for further details.

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Venoms

Many patients with suspected honey bee and/or common wasp specific IgE test positive to both species when using extract testing. True double allergic reactivity to both bee and wasp is not clinically common. In many cases double venom IgE positivity can be caused by cross-reactions to CCDs[1-5]. Recombinant venom components do not carry CCD and therefore provide greater diagnostic specificity, useful when making decisions such as to start AIT[1-7]. Ves v 1 and Ves v 5 are major allergens from common wasp and Pol d 5 is a marker for sensitization to paper wasp. The picture for honey bee sensitivity seems more complex than for wasp and can involve more varied sensitization patterns to major components. Api m 1, Api m 2, Api m 3, Api m 5 and Api m 10 are all major allergens within bee venom allergy. It has recently been shown that using an increasing number of bee components can improve diagnostic sensitivity[1-7].
Low level specific IgE below 0.35 kU_A/l can be relevant when using components and may be indicative of venom allergy, so measuring down to 0.1 kU_A/l can be important[1,6].

Patients with suspected venom allergy should also be tested with ImmunoCAP Tryptase[5,8-9]. Patients with high basal levels of tryptase should be investigated for mastocytosis since these patients have higher risk for severe reactions during venom immunotherapy[5,8-9].

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Latex

Primary latex allergy should be identified using specific allergen components as many positive extract test results arise as a result of cross-reactive pollen sensitization involving profilin, CCDs or PR-10 allergens[1-6]. The association of latex allergy and allergy to plant-derived foods is referred to as the latex-fruit syndrome and includes a large number of plant foods such as avocado, banana, chestnut, kiwi, peach, tomato, potato and bell pepper. The latex allergen Hev b 6 is considered the main culprit in this syndrome[1-2].

IgE antibodies to Hev b 1, Hev b 3, Hev b 5 and Hev b 6 are markers for primary latex allergy[1-6]. Sensitization to these components is frequent in surgery-related latex-allergy, especially among children having undergone multiple and extensive surgery, such as those with spina bifida. Sensitization to Hev b 5 and Hev b 6 is associated with occupational exposure to latex e.g. in healthcare workers and food-handling personnel using latex gloves[1-5]. Latex allergens Hev b 8 (profilin) and Hev b 6 can be used for examining cross-reactivity to pollen and plant foods, respectively[1-4]. If an exclusive sensitization to the profilin Hev b 8 is seen, allergic symptoms to latex are hardly to be expected[5,6].

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Immunotherapeutics – Aeroallergens and venoms

Understanding cross-sensitization and identifying the right allergen source

Clinically it is obviously important to correctly identify the allergen source causing symptoms before starting immunotherapy and this is not always easy[1-6]. Patients can be cross-sensitized to several allergen species; therefore sometimes it is not clear what the disease-eliciting source is. This applies to pollen allergies as well as to animal, dust mite and venom allergy. Tests with molecular allergens can help streamline the identification process[1-6]. Specific molecules from, for example, grass 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[3, 6-7]. Immunotherapy products vary from manufacturer to manufacturer; they contain molecules from the allergen source. But which ones and in what quantity? Most products contain larger quantities of the major allergens such as Bet v 1 in birch or Phl p 1 and Phl p 5 in timothy grass and Der p 1 in mite extracts, while sometimes much lower quantities of other allergens are included[7]. Patients who are positive only to the minor allergens are therefore less likely to respond satisfactorily[1-7,10-11].

Many patients with suspected venom allergy can be positive for both bee and wasp whole allergens. Double positivity can be caused by CCDs rather than true double sensitization[1-3,8-11]. ImmunoCAP recombinant venom components are CCD-free, which enables the physician to distinguish between positivity from cross-reactions and true venom allergy before selecting the right immunotherapeutic solution. Api m 3 and Api m 10 can be absent or underrepresented in VIT extracts and venom AIT in patients sensitized to these components may be less efficient[10-11].

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Common questions regarding allergen 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 kU_A /L, the same as normal whole extract sources such as cat, peanut etc.

How many ImmunoCAP Allergen Components are available?

There are currently over 100 tests with allergen components in the product range. A list is included in this guide, however availability may differ between countries.

For each allergen source how do I know that the ImmunoCAP Allergen Components represent the whole allergen extract?

Generally speaking they don't. For example, there are over 30 proteins reported in the peanut extract, many not clinically relevant or with unknown relevance. The field of molecular allergology is ever-expanding as we gain further scientific information and knowledge. Thermo Fisher Scientific supplies (Phadia AB is manufacturer) between 2-4 new components every year. Since 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' sensitizations.

What is ImmunoCAP ISAC?

ImmunoCAP ISAC is a microarray chip which tests for IgE to 112 allergen components simultaneously. It is a multiplex test giving semi-quantitative results on a patient's

allergen component sensitization profile. It has been found useful for the diagnosis of the following, but this list is not exhaustive: complex allergy, OAS, and cases of multi-sensitization, idiopathic anaphylaxis and high total IgE patients. More information on ImmunoCAP ISAC is available in Go Molecular, Book 2.

Where can I get access to ImmunoCAP ISAC?

Your local immunology laboratory may have ImmunoCAP ISAC in-house, otherwise the lab 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 an ImmunoCAP Whole Allergen test result that is negative and an ImmunoCAP Allergen Component test result that is positive (from the same source)?

This is possible in some cases. The whole allergen contains a mix of proteins, representing the natural composition at the source, while the allergen component is one single pure protein. Overall the component tests give higher 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 immunogenic protein from an allergen source e.g. Ara h 2 from peanut.

Cross-reactivity/Cross-sensitization – IgE antibodies directed against one allergen may cross-react to structurally related allergens from other allergen sources. Cross-reactive antibodies can cause a variety of different clinical outcomes.

Epitope – Defined substructure of a protein to which an antibody binds.

ImmunoCAP – an in vitro test for the measurement of specific IgE antibodies. ImmunoCAP is one of the market leaders and has been established for several decades. ImmunoCAP is also available for testing for other immunoglobulins (e.g. IgG4/ IgG).

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

Primary sensitizing 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 – Major allergen components are those to which at least 50% of relevant patients are sensitized. 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 sensitization – IgE antibodies directed to a primary sensitizer cross-react due to the similarity of the proteins/allergens and give rise to cross-reactive sensitization. This occurs in food-pollen syndrome for example, when an individual is sensitized to birch PR-10 (Bet v1) and the IgE antibodies then cross-react to peanut PR-10 (Ara h 8).

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

Educational resources

allergyai.com – Home Page of Immunodiagnostics, Thermo Fisher Scientific

allergen.org – International Union for Immunological Sciences/WHO Allergen Database

Matricardi PM et al. EAACI Molecular Allergology User's Guide. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology. 2016;27 Suppl 23:1-250.

Kleine-Tebbe J and Jakob T Editors: Molecular Allergy Diagnostics. Innovation for a Better Patient Management. Springer International Publishing Switzerland 2017. ISBN 978-3-319-42498-9 ISBN 978-3-319-42499-6 (eBook), DOI 10.1007/978-3-319-42499-6

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Using ImmunoCAP Allergen Component tests

The term 'ImmunoCAP Allergen Component' is used for singleplex ImmunoCAP products based on molecular allergens purified from either their natural source (native) or biotechnologically produced as recombinant proteins bound to the conventional ImmunoCAP solid phase.

By using tests for single allergen components as a complement to more traditional specific IgE antibody tests, further clinically relevant and quantitative information can be gained as an aid to the physician in making a diagnosis of allergy.

Allergen components are also available in a multiplex microarray format, ImmunoCAP ISAC. Here each test contains 112 components giving 112 semi-quantitative specific IgE results, thus presenting a snapshot of the patient's complete sensitization profile in one test.

More information on ImmunoCAP ISAC is available in Book 2.

The interpretation of sensitizations to allergen components that is described in this book, (as well as in book 2) is the same for both single and multiplex formats.

ImmunoCAP Allergen Components, singleplex as well as multiplex, are useful tools for the physician when investigating and explaining allergic reactions in more detail and to determine if cross-reacting IgE antibodies or primary sensitization causes them. However as all test results they must be evaluated by the physician together with the clinical history of the individual patient.

Presence of allergen specific IgE implies a risk of allergic disease and generally the higher the level of IgE antibodies the higher the probability of a clinically manifest allergic reaction[1-5]. However, due to differences in individual patient sensitivities identical results for the same allergens may not be associated with clinically equivalent manifestations. This may also be true for one individual patient at different occasions due to presence or absence of reaction promoting cofactors[1-5].

Absence of detectable allergen specific IgE antibodies does not necessarily exclude the potential for an allergy-like reaction[1,2].

Limitations of ImmunoCAP products test results:
Samples with results below limit of quantitation obtained with ImmunoCAP Allergen Components are recommended

to be tested with the corresponding extract based ImmunoCAP Allergen and/or additional relevant ImmunoCAP Allergen Components, if not already performed and a clinical indication is present. The extract based testing can cover additional allergen components present in the allergen source material to which the patient may be sensitized, but which are not presently available as ImmunoCAP Allergen Components or in ImmunoCAP ISAC.

A result below limit of quantitation obtained with an extract based ImmunoCAP Allergen never excludes the possibility of obtaining measurable concentrations of specific IgE when testing with ImmunoCAP Allergen Components from the same allergen source. This is due to the fact that some components may be present in very low amounts in the natural extract.

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ImmunoCAP Allergen Component list*

Product description	Latin name	Code	Size	Art. no.	Barcode
Grass pollen					
Cyn d 1 Bermuda grass	*Cynodon dactylon*	g216	10	14-4972-01	CFA
rPhl p 1 Timothy	*Phleum pratense*	g205	10	14-5234-01	BSU
rPhl p 2 Timothy	*Phleum pratense*	g206	10	14-5235-01	C0K
nPhl p 4 Timothy	*Phleum pratense*	g208	10	14-5288-01	C0L
rPhl p 5b Timothy	*Phleum pratense*	g215	10	14-5338-01	BV3
rPhl p 6 Timothy	*Phleum pratense*	g209	10	14-5289-01	BSV
rPhl p 7 Timothy	*Phleum pratense*	g210	10	14-5290-01	BSW
rPhl p 11 Timothy	*Phleum pratense*	g211	10	14-5291-01	BSX
rPhl p 12 Profilin, Timothy	*Phleum pratense*	g212	10	14-5292-01	BSY
rPhl p 1, rPhl p 5b Timothy	*Phleum pratense*	g213	10	14-5312-01	BU1
rPhl p 7, rPhl p 12 Timothy	*Phleum pratense*	g214	10	14-5313-01	BU2
Weed pollen					
nAmb a 1 Ragweed	*Ambrosia artemisiifolia (A. elatior)*	w230	10	14-4969-01	CF8
nArt v 1 Mugwort	*Artemisia vulgaris*	w231	10	14-4970-01	CF9
nArt v 3 LTP, Mugwort	*Artemisia vulgaris*	w233	10	14-4983-01	CJ2
rPar j 2 LPT, Wall pellitory	*Parietaria judaica*	w211	10	14-5311-01	C2M
rPla l 1 Plantain	*Plantago lanceolata*	w234	10	14-5751-01	D1H
nSal k 1 Saltwort	*Salsola kali*	w232	10	14-4978-01	CFE
Tree pollen					
rBet v 1 PR-10, Birch	*Betula verrucosa*	t215	10	14-5225-01	BPV
rBet v 2 Profilin, Birch	*Betula verrucosa*	t216	10	14-5226-01	BR1
rBet v 4 Birch	*Betula verrucosa*	t220	10	14-5287-01	BT7
rBet v 6 Birch	*Betula verrucosa*	t225	10	14-5345-01	CF1
rBet v 2, rBet v 4 Birch	*Betula verrucosa*	t221	10	14-5310-01	BU0
nCup a 1 Cypress	*Cupressus arizonica*	t226	10	14-4977-01	CFD
rOle e 1 Olive	*Olea europaea*	t224	10	14-5705-01	CTC
nOle e 7 LTP, Olive	*Olea europeae*	t227	10	14-4993-01	CKT
rOle e 9, Olive	*Olea europeae*	t240	10	14-4999-01	CTZ
rPla a 1 Maple leaf sycamore, London plane	*Platanus acerifolia*	t241	10	14-5957-01	D2H

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Product description	Latin name	Code	Size	Art. no.	Barcode
Microorganisms					
rAlt a 1	*Alternaria alternata*	m229	10	14-5346-01	CE0
rAsp f 1	*Aspergillus fumigatus*	m218	10	14-5293-01	BPL
rAsp f 2	*Aspergillus fumigatus*	m219	10	14-5294-01	BPM
rAsp f 3	*Aspergillus fumigatus*	m220	10	14-5295-01	BT4
rAsp f 4	*Aspergillus fumigatus*	m221	10	14-5296-01	BPN
rAsp f 6	*Aspergillus fumigatus*	m222	10	14-5297-01	BPP
Epidermals and animal proteins					
nBos d 6 BSA, Cow	*Bos spp.*	e204	10	14-5009-01	BRV
rCan f 1 Dog	*Canis familiaris*	e101	10	14-4955-01	CBN
rCan f 2 Dog	*Canis familiaris*	e102	10	14-4956-01	CBP
nCan f 3 Dog serum albumin	*Canis familiaris*	e221	10	14-5241-01	C14
rCan f 4 Dog	*Canis familiaris*	e229	10	14-5755-01	CZY
rCan f 5 Dog	*Canis familiaris*	e226	10	14-4998-01	CMZ
rCan f 6 Dog	*Canis familiaris*	e230	10	14-6081-01	E2X
rFel d 1 Cat	*Felis domesticus*	e94	10	14-4905-01	BY0
rFel d 2 Cat serum albumin	*Felis domesticus*	e220	10	14-5240-01	BRX
rFel d 4 Cat	*Felis domesticus*	e228	10	14-5702-01	CT9
rFel d 7 Cat	*Felis domesticus*	e231	10	14-6082-01	E2Y
rEqu c 1 Horse	*Equus caballus*	e227	10	14-5700-01	CN7
nSus s Pig serum albumin, Swine	*Sus scrofa*	e222	10	14-5242-01	C36
Mites					
rDer p 1 House dust mite	*Dermatophagoides pteronyssinus*	d202	10	14-5996-01	DP4
rDer p 2 House dust mite	*Dermatophagoides pteronyssinus*	d203	10	14-4967-01	CG2
rDer p 10 Tropomyosin, House dust mite	*Dermatophagoides pteronyssinus*	d205	10	14-4985-01	CG5
rDer p 23 House dust mite	*Dermatophagoides pteronyssinus*	d209	10	14-6040-01	DWU
Venoms					
rApi m 1 Phospholipase A2, Honey bee	*Apis mellifera*	i208	10	14-4987-01	CJ7
rApi m 2 Hyaluronidase, Honey bee	*Apis mellifera*	i214	10	14-6014-01	DUD
rApi m 3, Acid phosphatase, Honey bee	*Apis mellifera*	i215	10	14-6015-01	DUC
rApi m 5 Dipeptidyl peptidase, Honey bee	*Apis mellifera*	i216	10	14-6016-01	DUB
rApi m 10 Icarapin, Honey bee	*Apis mellifera*	i217	10	14-6004-01	DR0
rVes v 1 Phospholipase A1, Common wasp	*Vespula vulgaris*	i211	10	14-4995-01	CMR
rVes v 5 Common wasp	*Vespula vulgaris*	i209	10	14-4992-01	CJ8
rPol d 5 Paper wasp	*Polistes dominulus*	i210	10	14-4994-01	CJ9
Occupational					
rHev b 1 Latex	*Hevea brasiliensis*	k215	10	14-5324-01	C20
rHev b 3 Latex	*Hevea brasiliensis*	k217	10	14-5326-01	C2A
rHev b 5 Latex	*Hevea brasiliensis*	k218	10	14-5327-01	C1Z
rHev b 6.02 Latex	*Hevea brasiliensis*	k220	10	14-5329-01	C22
rHev b 8 Profilin, Latex	*Hevea brasiliensis*	k221	10	14-5330-01	C1V
rHev b 11 Latex	*Hevea brasiliensis*	k224	10	14-5333-01	C29

Product description	Latin name	Code	Size	Art. no.	Barcode
Occupational / Enzymes					
nAna c 2 Bromelain, Pineapple	*nAna c 2 Bromelain, Pineapple*	k202	10	14-5127-01	BT1
nAsp o 21 alpha-amylase	*nAsp o 21 alpha-amylase*	k87	10	14-4370-01	595
nGal d 4 Lysozyme, Egg	*nGal d 4 Lysozyme, Egg*	k208	10	14-5128-01	C0T
nSus s Pepsin, Swine	*nSus s Pepsin, Swine*	k213	10	14-5258-01	C3B
Foods					
rAct d 8 PR-10, Kiwi	*Actinidia deliciosa*	f430	10	14-4984-01	CG7
rAna o 3 Cashew nut	*Anacardium occidentale*	f443	10	14-5760-01	D0W
rApi g 1.01 PR-10, Celery	*Apium graveolens*	f417	10	14-4957-01	CBR
rAra h 1 Peanut	*Arachis hypogaea*	f422	10	14-4963-01	CDF
rAra h 2 Peanut	*Arachis hypogaea*	f423	10	14-4964-01	CDG
rAra h 3 Peanut	*Arachis hypogaea*	f424	10	14-4965-01	CDH
rAra h 6 Peanut	*Arachis hypogaea*	f447	10	14-6041-01	DYU
rAra h 8 PR-10, Peanut	*Arachis hypogaea*	f352	10	14-5341-01	CEZ
rAra h 9 LTP, Peanut	*Arachis hypogaea*	f427	10	14-4980-01	CFC
rBer e 1 Brazil nut	*Bertholletia excelsa*	f354	10	14-5343-01	CDS
rSes i 1, Sesame seed	*Sesamum indicum*	f449	10	14-6109-01	E7M
nBos d 4 alpha-lactalbumin, Milk	*Bos spp.*	f76	10	14-4522-01	CTP
nBos d 5 beta-lactoglobulin, Milk	*Bos spp.*	f77	10	14-4523-01	CTR
nBos d 8 Casein, Milk	*Bos spp.*	f78	10	14-4524-01	CTS
rCor a 1 PR-10, Hazel nut	*Corylus avellana*	f428	10	14-4981-01	CFB
rCor a 8 LTP, Hazel nut	*Corylus avellana*	f425	10	14-4968-01	CDP
nCor a 9, Hazel nut	*Corylus avellana*	f440	10	14-5758-01	D0M
rCor a 14, Hazel nut	*Corylus avellana*	f439	10	14-5754-01	CZP
rCyp c 1 Carp	*Cyprinus carpio*	f355	10	14-5344-01	CF0
rGad c 1 Cod	*Gadus morhua*	f426	10	14-4971-01	CEY
nGal d 1 Ovomucoid, Egg	*Gallus spp.*	f233	10	14-4805-01	904
nGal d 2 Ovalbumin, Egg	*Gallus spp.*	f232	10	14-4804-01	903
nGal d 3 Conalbumin, Egg	*Gallus spp.*	f323	10	14-5222-01	C18
rGly m 4 PR-10, Soy	*Glycine max*	f353	10	14-5340-01	CDR
nGly m 5 beta-conglycinin, Soy	*Glycine max*	f431	10	14-4990-01	CLV
nGly m 6 Glycinin	*Glycine max*	f432	10	14-4991-01	CLU
rJug r 1 Walnut	*Juglans regia*	f441	10	14-5762-01	D0T
rJug r 3 LTP, Walnut	*Juglans regia*	f442	10	14-5954-01	D11
rMal d 1 PR-10, Apple	*Malus domestica*	f434	10	14-5703-01	CWR
rMal d 3 LTP, Apple	*Malus domestica*	f435	10	14-5704-01	CWS
rPen a 1 Tropomyosin, Shrimp	*Penaeus aztecus*	f351	10	14-5335-01	C11
rPru p 1 PR-10, Peach	*Prunus persica*	f419	10	14-4960-01	CBV

Product description	Latin name	Code	Size	Art. no.	Barcode
Foods continued					
rPru p 3 LTP, Peach	*Prunus persica*	f420	10	14-4961-01	CBW
rPru p 4 Profilin, Peach	*Prunus persica*	f421	10	14-4962-01	CBX

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rPru p 7, Peach	*Prunus persica*	f454	10	14-6086-01	E3Z
rTri a 14 LTP, Wheat	*Triticum aestivum*	f433	10	14-5701-01	CN6
rTri a 19 Omega-5 Gliadin, Wheat	*Triticum aestivum*	f416	10	14-4954-01	C8H
Gliadin		f98	10	14-5752-01	CXG

Miscellaneous					
nGal-alpha-1,3-Gal (alpha-Gal) Thyroglobulin, bovine		o215	10	14-5997-01	DPC
MUXF3 CCD, Bromelain		o214	10	14-5339-01	CJU

ImmunoCAP ISAC$_{112i}$ Chip Allergen Components

Allergen component	Allergen source common name	Latin name	Protein group
Food allergens			
Gal d 1	Egg white	*Gallus domesticus*	Ovomucoid
Gal d 2	Egg white	*Gallus domesticus*	Ovalbumin
Gal d 3	Egg white	*Gallus domesticus*	Conalbumin/Ovotransferrin
Gal d 5	Egg yolk/chicken meat	*Gallus domesticus*	Livetin/Serum albumin
Bos d 4	Cow's milk	*Bos domesticus*	Alpha-lactalbumin
Bos d 5	Cow's milk	*Bos domesticus*	Beta-lactoglobulin
Bos d 6	Cow's milk and meat	*Bos domesticus*	Serum albumin
Bos d 8	Cow's milk	*Bos domesticus*	Casein
Bos d lactoferrin	Cow's milk	*Bos domesticus*	Transferrin
Gad c 1	Cod	*Gadus callarias*	Parvalbumin
Pen m 1	Shrimp	*Penaeus monodon*	Tropomyosin
Pen m 2	Shrimp	*Penaeus monodon*	Arginine kinase
Pen m 4	Shrimp	*Penaeus monodon*	Sarcoplasmic Ca-binding protein
Ana o 2	Cashew nut	*Anacardium occidentale*	Storage protein, 11S globulin
Ana 0 3	Cashew nut	*Anacardium occidentale*	Storage Protein, 2S albumin
Ber e 1	Brazil nut	*Bertholletia excelsa*	Storage protein, 2S albumin
Cor a 1.0401	Hazelnut	*Corylus avellana*	PR-10 protein
Cor a 8	Hazelnut	*Corylus avellana*	Lipid transfer protein (nsLTP)
Cor a 9	Hazelnut	*Corylus avellana*	Storage protein, 11S globulin
Cor a 14	Hazelnut	*Corylus avellana*	Storage Protein, 2S albumin
Jug r 1	Walnut	*Juglans regia*	Storage protein, 2S albumin
Jug r 3	Walnut	*Juglans regia*	Lipid transfer protein (nsLTP)
Ses i 1	Sesame seed	*Sesamum indicum*	Storage protein, 2S albumin
Ara h 1	Peanut	*Arachis hypogaea*	Storage protein ,7S globulin
Ara h 2	Peanut	*Arachis hypogaea*	Storage protein, 2S albumin
Ara h 3	Peanut	*Arachis hypogaea*	Storage protein, 11S globulin
Ara h 6	Peanut	*Arachis hypogaea*	Storage protein, 2S albumin
Ara h 8	Peanut	*Arachis hypogaea*	PR-10 protein
Ara h 9	Peanut	*Arachis hypogaea*	Lipid transfer protein (nsLTP)
Gly m 4	Soybean	*Glycine max*	PR-10 protein
Gly m 5	Soybean	*Glycine max*	Storage protein, Beta-conglycinin
Gly m 6	Soybean	*Glycine max*	Storage protein, Glycinin
Fag e 2	Buckwheat	*Fagopyrum esculentum*	Storage protein, 2S albumin
Tri a 14	Wheat	*Triticum aestivum*	Lipid transfer protein (nsLTP)
Tri a 19.0101	Wheat	*Triticum aestivum*	Omega-5 gliadin
Tri a aA_TI	Wheat	*Triticum aestivum*	
Act d 1	Kiwi	*Actinidia deliciosa*	
Act d 2	Kiwi	*Actinidia deliciosa*	Thaumatine-like protein
Act d 5	Kiwi	*Actinidia deliciosa*	
Act d 8	Kiwi	*Actinidia deliciosa*	PR-10 protein
Api g 1	Celery	*Apium graveolens*	PR-10 protein
Mal d 1	Apple	*Malus domestica*	PR-10 protein
Pru p 1	Peach	*Prunus persica*	PR-10 protein
Pru p 3	Peach	*Prunus persica*	Lipid transfer protein (nsLTP)

Allergen component	Allergen source common name	Latin name	Protein group
Aeroallergens			
Cyn d 1	Bermuda grass	*Cynodon dactylon*	Grass group 1
Phl p 1	Timothy grass	*Phleum pratense*	Grass group 1
Phl p 2	Timothy grass	*Phleum pratense*	Grass group 2
Phl p 4	Timothy grass	*Phleum pratense*	
Phl p 5b	Timothy grass	*Phleum pratense*	Grass group 5
Phl p 6	Timothy grass	*Phleum pratense*	
Phl p 7	Timothy grass	*Phleum pratense*	Polcalcin
Phl p 11	Timothy grass	*Phleum pratense*	
Phl p 12	Timothy grass	*Phleum pratense*	Profilin
Aln g 1	Alder	*Alnus glutinosa*	PR-10 protein
Bet v 1	Birch	*Betula verrucosa*	PR-10 protein
Bet v 2	Birch	*Betula verrucosa*	Profilin
Bet v 4	Birch	*Betula verrucosa*	Polcalcin
Cor a 1.0101	Hazel pollen	*Corylus avellana*	PR-10 protein
Cry j 1	Japanese ceder	*Cryptomeria japonica*	
Cup a 1	Cypress	*Cupressus arizonica*	
Ole e 1	Olive	*Olea europaea*	
Ole e 7	Olive	*Olea europaea*	Lipid transfer protein (nsLTP)
Ole e 9	Olive	*Olea europaea*	
Pla a 1	Plane tree	*Platanus acerifolia*	
Pla a 3	Plane tree	*Platanus acerifolia*	Lipid transfer protein (nsLTP)
Amb a 1	Ragweed	*Ambrosia artemisiifolia*	
Art v 1	Mugwort	*Artemisia vulgaris*	
Art v 3	Mugwort	*Artemisia vulgaris*	Lipid transfer protein (nsLTP)
Che a 1	Goosefoot	*Chenopodium album*	
Mer a 1	Annual mercury	*Mercurialis annua*	Profilin
Par j 2	Wall pellitory	*Parietaria judaica*	Lipid transfer protein (nsLTP)
Pla l 1	Plantain (English)	*Plantago lanceolata*	
Sal k 1	Saltwort	*Salsola kali*	
Can f 1	Dog	*Canis familiaris*	Lipocalin
Can f 2	Dog	*Canis familiaris*	Lipocalin
Can f 3	Dog	*Canis familiaris*	Serum albumin
Can f 4	Dog	*Canis familiaris*	Lipocalin
Can f 5	Dog	*Canis familiaris*	Arginine esterase
Can f 6	Dog	*Canis familiaris*	Lipocalin
Equ c 1	Horse	*Equus caballus*	Lipocalin
Equ c 3	Horse	*Equus caballus*	Serum albumin
Fel d 1	Cat	*Felis domesticus*	Uteroglobin
Fel d 2	Cat	*Felis domesticus*	Serum albumin
Fel d 4	Cat	*Felis domesticus*	Lipocalin
Mus m 1	Mouse	*Mus musculus*	Lipocalin
Alt a 1	Alternaria	*Alternaria alternata*	
Alt a 6	Alternaria	*Alternaria alternata*	Enolase
Asp f 1	Aspergillus	*Aspergillus fumigatus*	
Asp f 3	Aspergillus	*Aspergillus fumigatus*	
Asp f 6	Aspergillus	*Aspergillus fumigatus*	Mn superoxide dismutase
Cla h 8	Cladosporium	*Cladosporium herbarum*	
Blo t 5	House dust mite	*Blomia tropicalis*	
Der f 1	House dust mite	*Dermatophagoides farinae*	
Der f 2	House dust mite	*Dermatophagoides farinae*	
Der p 1	House dust mite	*Dermatophagoides pteronyssinus*	
Der p 2	House dust mite	*Dermatophagoides pteronyssinus*	
Der p 10	House dust mite	*Dermatophagoides pteronyssinus*	Tropomyosin
Der p 23	House dust mite	*Dermatophagoides pteronyssinus*	Peritrophin-like protein
Lep d 2	Storage mite	*Lepidoglyphus destructor*	

Aeroallergens continued overleaf...

Allergen component	Allergen source common name	Latin name	Protein group
Aeroallergens continued			
Bla g 1	Cockroach	*Blattella germanica*	
Bla g 2	Cockroach	*Blattella germanica*	
Bla g 5	Cockroach	*Blattella germanica*	
Bla g 7	Cockroach	*Blattella germanica*	Tropomyosin
Other			
Ani s 1	Anisakis	*Anisakis simplex*	
Ani s 3	Anisakis	*Anisakis simplex*	Tropomyosin
Hev b 1	Latex	*Hevea brasiliensis*	
Hev b 3	Latex	*Hevea brasiliensis*	
Hev b 5	Latex	*Hevea brasiliensis*	
Hev b 6.01	Latex	*Hevea brasiliensis*	
Hev b 8	Latex	*Hevea brasiliensis*	Profilin
Gal-alpha-1,3-Gal	Alpha gal		Thryoglobulin
MUXF3	Sugar epitope from Bromelain		CCD-marker

Notes

Notes

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