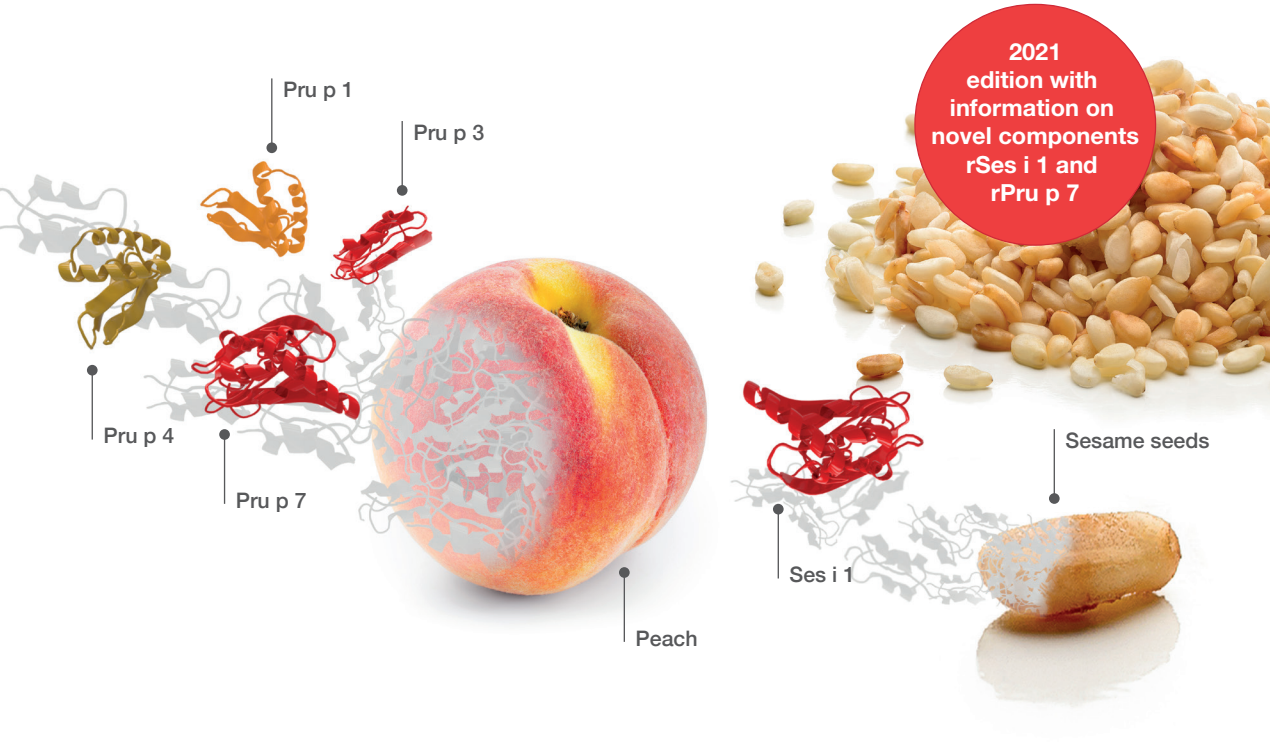
thermoscientific



Go molecular!

A clinical reference guide to molecular allergy

Part 2: The allergen components

Revised and updated 2nd edition (2021)

ThermoFisher SCIENTIFIC

Preface

In the original 2013 edition of Go Molecular, I produced a straight forward clinical reference guide book to describe common allergens and their constituent components. This guide is an update to the original but keeps the focus on understanding component test results, as well as what tests are actually commercial available (since this is an important practical aspect of molecular allergy!).

Since 2013 the science of molecular allergy has exploded with many new studies both using single and multiplex allergen testing formats. There is a lot of new clinical evidence to consider and new tests available. In 2019, I added in updates of new ImmunoCAP™ Allergen Component tests that became available that year, Cat (Fel d 7), Dog (Can f 4 and Can f 6) and Dust mite (Der p 23). In this latest update for 2021, I have included new test peach, rPru p 7, GRP as well as the interesting sesame Ses i 1, 2S albumin, both tests have the potential to make big impacts in the clinic.

Beyond the new science and products, the content in this 2nd edition of Go Molecular has been aimed to provide improved diagnostic explanations in the form of tables, with concise clinical interpretation comments. This includes overviews of aero-allergen components, an introduction to micro array, as well as new information on diagnostic gaps regarding certain food components.

If you need further supporting information relating to molecular allergy then I can recommend visiting our webpage: **allergyai.com.**

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

172050.AL.EU, INT, JP1.EN.v1.21

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 optimise 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 sensitisation 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

Since the last version of this book testing with allergen components has become a more standard diagnostic tool, providing an essential part of an allergy diagnosis work-up. Molecular allergology has refined the way that clinicians tailor their approach to patient management by redefining the patient diagnostic journey. Allergen components have made understanding allergy more scientific, moving towards precision medicine. This helps improve the understanding of a patient's true clinical reactivity, as well as making decisions to improve their quality of life.

Tests incorporating allergen components are defined entities, in that you know exactly what allergen protein you have in the test. Sometimes allergen component protein is present in a higher amount in an allergen component test when compared to a corresponding extract based test. This can make allergen component tests analytically even more sensitive and specific at measuring important IgEs of interest.

By using tests with allergen components you add another tool to the diagnostic armoury, which may make it possible to understand more about the underlying allergies. Tests with allergen components are not diagnostic 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 always be used in conjunction with an allergy-focused clinical history and physical examination and the diagnosis is then made by the physician.

Testing with allergen components helps in:

1. Understanding patient risk – adding confidence to your assessment[1-5]
2. Aiding in the selection of the proper treatment extract of Allergen Specific Immunotherapy (AIT) – useful for example in venom and aero-allergy patient selection[1-5]
3. Understanding cross-reactions between species – helping to understand multiple sensitizations e.g. in pollen food syndrome[1-5]

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 testing with allergen components more supporting information on molecular allergy is available at: **allergyai.com**.
Tests with allergen components 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.

Tests with allergen components differ as each test involves measuring specific IgE to pure single recombinant or native allergen proteins from a source. For example Pru p 3 is an nsLTP (non-specific lipid transfer protein) from peach. Antibodies produced by patients in response to specific allergen proteins can be measured using ImmunoCAP single (ImmunoCAP Allergen Component) or multiplex (ImmunoCAP™ ISAC) component tests. Both platforms therefore can be used to give an overview of the patients immunological response in their current allergy status.

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 on 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 components for further specificity, and as an aid in risk assessment if the whole allergen test for specific IgE is positive[1-5].

There is more information found in book 1 of this series or on the Thermo Fisher Scientific molecular allergy course: 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.
2. 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
3. Canonica GW et.al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 2013 Oct 3;6(1):17.
4. Wickman M. When allergies complicate allergies. Allergy 2005;60(S79):14-18.
5. van Hage M et.al. ImmunoCAP assays: Pros and cons in allergology. J Allergy Clin Immunol 2017;140:974-7.

What's in this guide book?

The purpose of this guide is to offer an 'all in one' reference to each allergen source and its components in a single practical booklet. Molecular allergology 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 helpful to make a risk assessment and what is actually available in the product range. I hope this booklet addresses these issues to make life a little easier!

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 whole allergens, allergen components and an aid to clinical interpretation of the main components can be found at: **allergyai.com**.

Major and minor allergen components

You will often find references and descriptions for major and minor allergens. Major allergen components are defined as allergens that account for over 50% of sensitization within an allergic population[1-2]. This may differ in different geographical regions due to different exposures to allergens. 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 pollen allergy the major allergen is Bet v 1 (PR-10-pathogenesis related family number 10), whilst a minor allergen is Bet v 2 (profilin)[1-2].

ImmunoCAP IgE test products available and new product updates

Thermo Fisher Scientific supplies (Phadia AB is the manufacturer) many exisiting and often new clinically relevant allergen components. Description of the products available at the time of going to press are listed in each section and on page 79. If you are interested in the latest updates and product releases register by contacting us at: **allergyai.com**.

Most of the information given in this guide is for single ImmunoCAP Allergen Components but is of course also valid for components on the multiplex product ImmunoCAP ISAC and may also be informative for whole extract allergens. The allergen code is also provided which can be useful when ordering from a testing laboratory. Whole allergens are still a useful sensitization guide and offer value by covering components from the allergen source not yet available as pure component tests. For example, we currently have six allergen components for peanut but over 15 have been described. We provide the most scientifically documented, clinically relevant component tests where possible. A common practice is to request testing for the whole allergen and ask the laboratory to reflex test for related components if the whole allergen is positive – a good use of time and resources.

Interpretation of results

In this guide, interpretation has been simplified as much as possible using a table format. The presence of allergen-specific IgE is a risk factor for allergy symptoms and a result higher than 0.1 kU_A /L indicates sensitization. Traditionally the higher the IgE antibody level the greater the likelihood of being symptomatic allergic. Some allergen components are associated with a much higher risk for severe symptoms, whilst some allergens are considered giving no or very low risk. A high-titre, high-risk allergen such as Ara h 2 or Cor a 14 would often carry a high risk for patients to suffer from severe symptoms. 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 abscence of reaction promoting cofactors[1-2].

Always consider test results in association with the clinical history for the individual patient.

References

References are inserted after each section.

A comprehensive overview of molecular allergology covering the introduction part is provided in:

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.
2. 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.

Allergen components from plant sources

Plant protein families are shared between species; the closer the species are related botanically the more similar the proteins are likely to 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 in the table below. These are Storage proteins, LTP, PR-10 and Profilin which are all proteins, and CCDs which are cross-reactive carbohydrate determinants:

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

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.
2. 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.
3. Canonica GW et.al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 2013 Oct 3;6(1):17.
4. Sastre J. Molecular diagnosis in allergy. Clin Exp Allergy 2010;40(10):1442-1460.
5. Treudler R. and Simon JC. Overview of component resolved diagnostics. Curr Allergy Asthma Rep 2013;13(1):110-117.

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 2 S 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	Storage proteins: 2S Albumin	Storage proteins: Vicilin-like 7S globulin	Storage proteins: Legumin-like 11 S globulin	Other
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

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.
2. 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.
3. Canonica GW et.al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 2013 Oct 3;6(1):17.
4. Sastre J. Molecular diagnosis in allergy. Clin Exp Allergy 2010;40(10):1442-1460.
5. Treudler R. and Simon JC. Overview of component resolved diagnostics. Curr Allergy Asthma Rep 2013;13(1):110-117.

www.allergen.org and www.allergome.org

Food allergens from plant sources

Peanut

Arachis hypogaea (Ara h)

Peanut allergy is of great interest and has increased in prevalence over the last few decades. Peanut is a problematic allergen source that is consumed in many different forms such as peanut butter, as snacks, in confectionery and in baked goods. Peanuts also yield cooking oils (both refined and crude, aromatic and non-aromatic) which may contain trace amount of allergens.

It is commonly accepted that Ara h 1, Ara h 2, Ara h 3 and Ara h 6 are major peanut allergens[1-4]. These allergens are heat stable and resistant to gastric acid fluid degradation. 2S albumin proteins such as Ara h 2 and Ara h 6 are considered to be the most important peanut allergens but IgE also to Ara h 1 and/or Ara h 3 increases risk of severe symptoms[1-5]. Ara h 2 and Ara h 6 allergen components provide the most accurate peanut test in terms of predictive value in the aid of diagnosis[1,4,6-12]. A minority of patients are mono-sensitised to Ara h 6 and not positive to Ara h 2; a combination of the two seems to provide the optimal performance[10,12].

IgE antibodies in 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[13-14]. IgE to timothy grass profilin (Phl p 12) can also cross-react with peanut profilin Ara h 5[13-14].

Available ImmunoCAP Allergen Products*

Peanut – Whole allergen – f13

Component		Code
rAra h 1	7S globulin, storage protein	f422
rAra h 2	2S albumin, storage protein	f423
rAra h 3	11S globulin, storage protein	f424
rAra h 6	2S albumin, storage protein	f447
rAra h 8	PR-10 protein	f352
rAra h 9	nsLTP	f427

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

f13	Ara h 1	Ara h 2	Ara h 3	Ara h 6	Ara h 8	Ara h 9	Interpretation
+/-	+						Indicates a primary peanut allergy. The patient is at high risk of severe, systemic symptoms, especially if Ara h 2 or Ara h 6 are positive.[1-14]
+/-		+					
+/-			+				
+/-				+			
+/-					+		The patient is at risk for local reactions, however, the probability of severe, systemic reactions is low.[13-14]
+/-						+	IgE to nsLTP is a risk marker of both systemic and local reactions. The patient may be reacting to other nsLTPs due to cross- reactions which can cause systemic symptoms to both cooked and uncooked foods.[13-14]

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Nicolaou N et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnosis. J Allergy Clin Immunol 2010;125:191-197.
2. Sicherer SH, et al. US prevalence of self-reported peanut, tree nut and sesame allergy: 11 year follow up. J Allergy Clin Immunol 2010:125;1322-1326.
3. Rona RJ et al. The prevalence of food allergy: a meta-analysis. J Allergy Clin Immunol 2007;120(3):638-646.
4. Lange L et al. Benefits and limitations of molecular diagnostics in peanut allergy. Allergo J Int 2014; 23:158–63.
5. Mortz CG et al. The prevalence of peanut sensitization and the association to pollen sensitization in a cohort of unselected adolescents – The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS). Paediatr Allergy Immunol 2005;16:501-506.
6. Eller E and Bindslev-Jensen C. Clinical value of component-resolved diagnostics in peanut-allergic patients. Allergy 2013;68(2):190-194.
7. 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.
8. 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.
9. Kukkonen AK et al. Ara h 2 and Ara 6 are the best predictors of severe peanut allergy: a double-blind placebo-controlled study. Allergy 2015 Oct;70(10):1239-45.
10. Rajput S et al. Allergy testing in predicting outcome of open food challenge to peanut. Journal of Allergy and Immunol 2017, published on line June 14.
11. Van Erp FC et.al. The IgE and basophil responses to Ara h 2 and Ara h 6 are good predictors of peanut allergy in children. Journal of Allergy and Immunol 2016. Available online August 8, 2016.
12. Klemans RJ et al. The diagnostic accuracy of specific IgE to Ara h 6 in adults is as good as Ara h 2. Allergy. 2014 Aug:69(8):1112-4.
13. 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.
14. 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.

Soybean

***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[1-2].

The presence of specific IgE to Gly m 5 and Gly m 6 may indicate primary soy allergy and risk of severe systemic reactions[3,4]. Gly m 8, a 2S Albumin, has recently been reported to be an important marker of soy allergy[5-7].Since 2002 soy allergic reactions have increasingly been linked to birch pollen sensitized individuals[8]. 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. However, with unprocessed soy in drinks (soy milk) and dietary protein powders (e.g. such as those sold 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 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)[7,9]. Gly m 4 content can be very low in extract- based tests. Therefore tests with Gly m 4 allergen component is recommended as supplement to testing with whole allergen[9].

Available ImmunoCAP Allergen Products*

Soybean – Whole allergen – f14

Component		Code
rGly m 4	PR-10 protein	f353
nGly m 5	β-conglycinin, storage protein	f431
nGly m 6	glycinin, storage protein	f432

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

f14	Gly m 4	Gly m 5	Gly m 6	Interpretation
+/-	+			A high allergen load of PR-10 can result in systemic symptoms. Consider checking how much consumption of soy has occurred (the allergen load) especially if the patient is Bet v 1 positive. For example does the patient regularly drink soya milk, perhaps in the pollen season?[7-10]
+/-		+		Indicates a primary soy allergy. The patient is at risk of severe, systemic symptoms[3-4,8,10]
+/-			+	

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. L'Hocine L and Boye J. Allergenicity of soybean: new developments in identification of allergenic proteins, cross-reactivities and hypoallergenization technologies. Crit Rev Food Sci Nutr 2007;47: 127–143.
2. Ballmer-Weber B et al. Soy allergy in perspective. Curr Opin Allergy Clin Immunol 2008;8:270– 275.
3. Holzhauser T et al. Soybean (Glycinemax) 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.
4. Ito T et al. IgE to Gly m 5 and Gly m 6 is associated with severe allergic reactions to soyabean in Japanese children. J Allergy Clin Immunol 2010;125;2 Suppl 1:AB88.
5. Kattan DJ and Sampson HJ. Clinical reactivity to soy is best identified by component testing to Gly m 8. J Allergy Clin Immunol Pract. 2015; 3(6):970–972.
6. Klemans RJ et al. Components in soy allergy diagnostics: Gly m 2S albumin has the best diagnostic value in adults. Allergy 2013;68:1396-1402.
7. Ebisawa M et al. Gly m 2S albumin is a major allergen with a high diagnostic value in soybean-allergic children. J Allergy Clin Immunol 2013;132:976-978 e1-5.
8. 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
9. 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(2):305-306.
10. 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.

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[1-2].

Cor a 9 and Cor a 14 are both storage proteins which are resistant to digestion and have been demonstrated in clinical studies to be major allergens which cause systemic symptoms[3-9]. 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[10]. 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[11-14].

Available ImmunoCAP Allergen Products*

Hazelnut – Whole allergen – f17

Component		Code
rCor a 1	PR-10	f428
rCor a 8	nsLTP	f425
nCor a 9	11S globulin, storage protein	f440
Cor a 14	2S albumin, storage protein	f439

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

f17	Cor a 1	Cor a 8	Cor a 9	Cor a 14	Interpretation
+/-	+				Probability is low for systemic reactions and local symptoms such as OAS are more likely. The patient may be reacting to other PR-10-containing pollens and plant foods due to cross-reactions[11-16]
+/-		+			Mixed allergy is possible, including systemic and local symptoms such as OAS. The patient may be reacting to other nsLTPs contained in other plant foods/pollens due to cross-reactions. This can cause systemic symptoms to both cooked and uncooked foods[10,15-16]
+/-			+		Primary hazelnut allergy, the patient is at high risk of severe, systemic allergy[3-9,15-16]
+/-				+	

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Beyer K et al. Identification of an 11S globulin as a major hazelnut food allergen in hazelnut-induced systemic reactions. J Allergy Clin Immunol 2002;110(3):517-523.
2. Ortolani C et al. Comparison of results of skin prick tests (with fresh foods and commercial food extracts) and RAST in 100 patients with oral allergy syndrome. J Allergy Clin Immunol 1989; 83(3):683-690.
3. Faber M et al. Cor a 14: Missing Link in the Molecular Diagnosis of Hazelnut Allergy? Int Arch Allergy Immunol 2014;164:200–206.
4. Kattan DJ et al. Clinical reactivity to hazelnut may be better identified by component testing than traditional testing methods. J Allergy Clin Immunol Pract 2014;2(5): 633–634.
5. Carraro S et al. COR a 14-specific IgE predicts symptomatic hazelnut allergy in children. Pediatric Allergy and Immunol 2016;27(3):322-4.
6. Eller E et al Cor a 14 is the superior serological marker for hazelnut allergy in children, independent of concomitant peanut allergy. Allergy 2016;71: 556–562.
7. Beyer K et al. Predictive values of component-specific IgE for the outcome of peanut and hazelnut food challenges in children. Allergy 2015;70: 90–98.
8. Masthoff L et al. Sensitization 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 Aug;132(2):393-9.
9. Brandström J et al.Basophil allergen threshold sensitivity and component-resolved diagnostics improve hazelnut allergy diagnosis. Clin Exp Allergy 2015;45(9):1412-8.
10. 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(2):423-428.
11. Hansen KS, et al. Roasted hazelnuts – allergenic activity evaluated by double-blind, placebo-controlled food challenge. Allergy 2003;58(2):132-138.
12. Anhoej C et al. Diagnostic evaluation of grass- and birch-allergic patients with oral allergy syndrome. Allergy 2001;56(6):548-552.
13. Kalyoncu AF, et al. Birch pollen related food hypersensitivity: as a para-occupational syndrome. Allergol Immunopathol (Madr) 1995;23(2):94-95.
14. Bindslev-Jensen C et al. Oral allergy syndrome: the effect of astemizole. Allergy 1991;46(8): 610-613 .
15. 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.
16. 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.

Walnut

***Juglans regia* (Jug r)**

Walnut is botanically closely related to pecan. Walnuts are often eaten as an ingredient in baked goods and as additive in other dishes e.g. meat, poultry, fish and pasta as well as in salads and ice cream. Walnut oil can be allergenic, although this depends on the extraction method and the purity of the end product[1].

Jug r 1, a 2S albumin storage protein that is resistant to digestion, has been associated with primary walnut allergy and systemic symptoms[2-4]. Presence of specific IgE antibodies to Jug r 3, an nsLTP, indicates that local symptoms as well as systemic reactions can occur[5-7].

Available ImmunoCAP Allergen Products*

Walnut – Whole allergen – f256

Component		Code
rJug r 1	2S albumin, storage protein	f441
rJug r 3	nsLTP	f442

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

f256	Jug r 1	Jug r 3	Interpretation
+/-	+		Primary walnut allergy, the patient is at high risk of severe, systemic allergy[2-4,8-11]
+/-		+	Mixed allergy is possible, including systemic and local symptoms such as OAS. The patient may be sensitized to other nsLTPs contained in other plant foods/ pollens due to cross-reactions which can cause systemic symptoms in cooked and uncooked foods[5-7,10-11]

**Walnut/Pecan share a high homology between proteins and the two allergens are highly cross reactive[2-3,8-9]. Patients sensitised to pecan nuts are very likely to also be IgE-reactive to walnut and vice versa. Jug r 1 and Jug r 3 are therefore risk markers for both pecan and walnut allergy.*

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Teuber SS et al. Allergenicity of gourmet nut oils processed by different methods. J Allergy Clin Immunol 1997;99(4):502-507.
2. Mew R et al. A retrospect study into the utility of allergen components in walnut allergy. Ped Allergy and Immunol 2016;27(7):750-752.
3. Costa J et al. Walnut allergens: molecular characterization, detection and clinical relevance. Clinical & Experimental Allergy, 2014 (44) 319–341.
4. Sato S et al. Jug r 1 sensitization is important in walnut-allergic children and youth. J Allergy Clin Immunol Pract. 2017;5(6):1784-1786.
5. Pastorello EA et al. Lipid transfer protein and vicilin are important walnut allergens in patients not allergic to pollen. J Allergy Clin Immunol 2004;114(4):908-914.
6. Egger M et al. The role of lipid transfer proteins in allergic diseases. Curr Allergy Asthma Rep 2010;20:326-335.
7. Romano A et al. Lipid transfer proteins: The most frequent sensitizer in Italian subjects with food-dependent exercise-induced anaphylaxis. Clin Exp Allergy 2012;42(11):1643-1653.
8. Teuber SS et al. Cloning and sequencing of a gene encoding a 2S albumin seed storage protein precursor from English walnut (Juglans regia), a major food allergen. J Allergy Clin Immunol 1998; 101:807–14.
9. Andorf S et al. Association of Clinical Reactivity with Sensitization to Allergen Components in Multifood-Allergic Children. J Allergy Clin Immunol. 2017;5(5):1325-1334.
10. 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.
11. 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

Cashew

***Anacardium occidentale* (Ana o)**

The cashew nut comes from the cashew nut tree, a member of the *Anacardiaceae* family, and is botanically 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 and is described as a primary cashew nut allergen associated with severe symtoms[1-4]. Significant cross-reactivity has been reported between pistachio nut and cashew nut[3,5-9]. Ana o 3 therefore can act as a risk marker for severe reactions also for pistachio.

The Rutaceae family (e.g. lemon, tangerine, orange) is closely related to the *Anacardiaceae* family to which cashew belongs. Cross-reactions of cashew-allergic individuals reacting to lemon and orange seeds hidden in juices and dressings have been described[10-11]. The cashew component Ana o 2, a vicilin-like storage protein, is available on ImmunoCAP ISAC.

Available ImmunoCAP Allergen Products*

Cashew – Whole allergen – f202

Component		Code
rAna o 3	2S albumin, storage protein	f443

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

f202	Ana o 3	Interpretation
+/-	+	Primary sensitization to cashew nut. The patient is at high risk of severe, systemic symptoms[1-4,12-13]

**Cashew and pistachio are closely botanically related and show extensive cross reactivity also between storage proteins. Patients sensitised to cashew Ana o 3 are most likely also reacting with symptoms to pistachio nuts[3,5-9].*

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Robotham JM et al. Ana o 3, an important cashew nut (Anacardium occidentale L.) allergen of the 2S albumin family. J Allergy Clin Immunol 2005;115(6):1284-1290.
2. Lange L et al Ana o 3-specific IgE is a good predictor for clinically relevant cashew allergy in children Allergy 2017;72(4):598-603.
3. Savvatianos S et al. Sensitization to cashew nut 2S albumin, Ana o 3, is highly predictive of cashew and pistachio allergy in Greek children J Allergy Clin Immunol 2015;136(1):192-4.
4. Van der Valk JMP et al. sIgE Ana o 1, 2 and 3 accurately distinguish tolerant from allergic children sensitized to cashew nuts Clin Exp Allergy 2016;47:113–120.
5. Fernandez C et al. Allergy to pistachio: cross reactivity between pistachio nut and other Anacardiaceae. Clin Exp Allergy 1995;(25):1254-1259.
6. Parra FM, et al. Pi stachio nut hypersensitivity: identification of pistachio nut allergens. Clin Exp Allergy 1993;23:996-1001.
7. Roux K et al. Tree nut allergens. Int Arch Allergy Immunology 2003;131:234-244.
8. Pastorello E et al. Sensitization to the major allergen of Brazil nut is correlated with the clinical expression of allergy. J Allergy Clin Immunol 1998;102(6):1021-1027.
9. Andorf S et al. Association of Clinical Reactivity with Sensitization to Allergen Components in Multifood-Allergic Children. J Allergy Clin Immunol. 2017;5(5):1325-1334.
10. Brandstrom J et al. IgE to novel citrus seed allergens among cashew-allergic children. Pediatric Allergy and Immunology 27 (2016)539–553.
11. O'Sullivan MD and Somerville C. Co-sensitization to orange seed and cashewnut. Ann Allergy Asthma Immunol 2011:107: 282–3.
12. 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.
13. 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

Brazil nut

***Bertholletia excelsa* (Ber e)**

Prevalence of Brazil nut allergy is becoming more common[1] and is associated with severe reactions[2-5]. A number of allergenic proteins has been isolated from Brazil nut. Like other tree nuts and seeds, Brazil nut contains storage proteins. Ber e 1 is a 2S albumin protein and a major allergen[1,10]. The 2S albumin group has been described extensively in many other legumes and tree nuts such as peanut (Ara h 2) and hazelnut (Cor a 14)[6].

Ber e 1, 2S albumin in Brazil nut has been found to be largely intact following gastric digestion[7,10]. High stability is a hallmark for allergens able to provoke a systemic allergic reaction in sensitized individuals[8-9]. A small UK study in 2015 identified rBer e 1 as an improvement in clinical test performance versus the whole allergen Brazil nut extract[1]. A further Brazil nut storage protein allergen, Ber e 2, an 11S globulin-like protein has also been identified.

Available ImmunoCAP Allergen Products*

Brazil nut – Whole allergen – f18

Component		Code
rBer e 1	2S albumin, storage protein	f354

*Complete product names on page 79.

Clinical relevance

Understanding primary Brazil nut allergy.

Interpreting the results

f18	rBer e 1	Interpretation
+/-	+	Major allergen. Primary sensitization to Brazil nut. The patient is at high risk of severe, systemic symptoms[1-7,11]

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Rayes H et al. Specific IgE to recombinant protein (Ber e 1) for the diagnosis of Brazil nut allergy Clinical & Experimental Allergy 2015;46, 654–656.
2. Pastorello EA et al. Sensitization to the major allergen of Brazil nut is correlated with the clinical expression of allergy. J Allergy Clin Immunol 1998;102:1021–1027.
3. de Leon MP el al. IgE cross-reactivity between the major peanut allergen Ara h 2 and tree nut allergens. Mol Immunol 2007;44:463–71.
4. Ewan PW. Clinical study of peanut and tree nut allergy in 62 consecutive patients: new features and associations. BMJ 1996;312:1074–8.
5. Pumphrey RSH and Stanworth SJ. The clinical spectrum of anaphylaxis in northwest England. Clin Exp Allergy 1996;26:1364–70.
6. 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.
7. Moreno FJ et al. Stability of the major allergen Brazil nut 2S albumin (Ber e 1) to physiologically relevant in vitro gastrointestinal digestion. FEBS J 2005;272(2):341-52.
8. Murtagh GJ et al. In vitro stability and immunoreactivity of the native and recombinant plant food 2S albumins Ber e 1 and SFA-8. Clin Exp Allergy 2003;33(8):1147-52.
9. Moreno FJ et al. Thermostability and in vitro digestibility of a purified major allergen 2S albumin (Ses i 1) from white sesame seeds (Sesamum indicum L). Biochim Biophys Acta 2005 Sep 25;1752(2):142-53.
10. Murtagh GJ et al. Stability of recombinant 2 S albumin allergens in vitro. Biochem Soc Trans 2001;30(6):913-5.
11. 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.

Sesame seed

Sesamum indicum (Ses i)

Sesame seed and oil are commonly used food ingredients around the world used for example as tahini paste or halva dessert, or as oil-based ingredients in pharmaceutical and cosmetic products. Sesame often cause severe reactions, and among common seeds and nuts, sesame was found to cause allergic symptoms with the highest severity[1]. Several storage proteins with high stability to heat and digestion have been identified in sesame[2]. Ses i 1 is a 2S albumin storage protein and a major allergen in sesame seed to which 55-100% of sesame allergic patients are sensitized[3,4]. Sesame allergy commonly co-exist with peanut and tree nut allergy and is about 50-60% in seed and nut multi-allergic patients[1,5]. Clinical cross-reactivity is however rarely reported with Ses i 1, but structural similarities with other 2S albumins in seeds and nuts such have been identifited[3,4,12].

In studies from Japan and USA, Ses i 1 is found to be a good candidate for assessing patients for primary sesame allergy with a better specificity compared to extract-based specific IgE to sesame[6-8]. Ses i 1 is also considered to be a better parameter for detecting positive outcomes of oral food challenge compared to extract-based sesame specific IgE and skin prick test[4,9-11].

Available ImmunoCAP Allergen Products*

Sesame seed – Whole allergen – f10

Component		Code
rSes i 1	2S albumin, storage protein	f449

*Complete product names on page 79.

Clinical relevance

Understanding primary Sesame seed allergy.

Interpreting the results

f10	rSes i 1	Interpretation
+/-	+	Major allergen. Primary sensitization to Sesame seed. The patient is at high risk of severe systemic symptoms[3-4, 6-11].

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Brough, H. A., J. C. Caubet, A. Mazon, D. Haddad, M. M. Bergmann, J. Wassenberg, V. Panetta, R. Gourgey, S. Radulovic, M. Nieto, A. F. Santos, A. Nieto, G. Lack and P. A. Eigenmann (2020). "Defining challenge-proven coexistent nut and sesame seed allergy: A prospective multicenter European study." J Allergy Clin Immunol 145(4): 1231-1239.
2. WHO/IUIS (2019). Allergen Nomenclature "Sesamum indicum - All Allergen", WHO/IUIS Allergen Nomenclature Sub-Committee.
3. Pastorello, E. A., E. Varin, L. Farioli, V. Pravettoni, C. Ortolani, C. Trambaioli, D. Fortunato, M. G. Giuffrida, F. Rivolta, A. Robino, A. M. Calamari, L. Lacava and A. Conti (2001). "The major allergen of sesame seeds (Sesamum indicum) is a 2S albumin." J Chromatogr B Biomed Sci Appl 756(1-2): 85-93.
4. Maruyama, N., T. Nakagawa, K. Ito, C. Cabanos, M. P. Borres, R. Movérare, A. Tanaka, S. Sato and M. Ebisawa (2016). "Measurement of specific IgE antibodies to Ses i 1 improves the diagnosis of sesame allergy." Clin Exp Allergy 46(1): 163-171.
5. Tuano, K. T., K. H. Dillard, D. Guffey and C. M. Davis (2016). "Development of sesame tolerance and cosensitization of sesame allergy with peanut and tree nut allergy in children." Ann Allergy Asthma Immunol 117(6): 708-710.
6. Borres, M., N. Maruyama, S. Sato and M. Ebisawa (2016). "Recent advances in component resolved diagnosis in food allergy." Allergology International 65.
7. Sato, S., N. Yanagida and M. Ebisawa (2018). "How to diagnose food allergy." Curr Opin Allergy Clin Immunol 18(3): 214-221.
8. Foong, R. X., J. A. Dantzer, R. A. Wood and A. F. Santos (2021). "Improving Diagnostic Accuracy in Food Allergy." J Allergy Clin Immunol Pract 9(1): 71-80.
9. Yanagida, N., Y. Ejiri, D. Takeishi, S. Sato, N. Maruyama, K. Takahashi, K. I. Nagakura, K. Ogura, T. Asaumi and M. Ebisawa (2019). "Ses i 1-specific IgE and sesame oral food challenge results." J Allergy Clin Immunol Pract 7(6): 2084-2086.e2084.
10. Saf, S., T. M. Sifers, M. G. Baker, C. M. Warren, C. Knight, K. Bakhl, J. D. Kattan, H. A. Sampson and A. Nowak-Wegrzyn (2020). "Diagnosis of Sesame Allergy: Analysis of Current Practice and Exploration of Sesame Component Ses i 1." J Allergy Clin Immunol Pract 8(5): 1681-1688.e1683.
11. Goldberg MR, Appel MY, Nachshon L, Holmqvist M, Epstein-Rigbi N, Levy MB et al. Combinatorial advantage of Ses i 1-specific IgE and Basophil Activation for diagnosis of Sesame Food Allergy. Pediatr Allergy Immunol. 2021 May 5. doi: 10.1111/pai.13533. Online ahead of print.
12. Kleine-Tebbe, J., T. Jacob and R. Hamilton (2017). Molecular Allergy Diagnostics Using IgE Singleplex Assays: Methodological and Practical Considerations. Molecular Allergy Diagnostics: Innovation for a Better Patient Management. J. Kleine-Tebbe and T. Jakob. Switzerland, Springer International Publishing: 152.

Fruits and *Rosaceae* Family

Fruit allergen sources are quite widespread but many fruit allergies are caused by members of the *Rosaceae* family and often are initiated by a primary sensitization to pollen[1]. LTPs are major allergen components in fruit and have often been considered to be more associated with Southern European regions[1], although recent studies have identified LTP allergy also in Central[2] and Northern Europe[2-3]. Due to high structural homology, Pru p 3 (nsLTP) can be a useful general marker for *Rosaceae* allergy[1] and is associated with systemic symptoms as well as oral allergy[4]. Furthermore patients sensitized to more than five LTPs often have a higher prevalence of food-induced systemic symptoms[5]. LTP levels are concentrated in the skin/fuzz and outer layers of fruits and by removing the peel exposure to the allergen can be reduced[1]. Patients sensitized to nsLTP without concomitant sensitization to profilin or PR-10's are prone to suffer from more severe symtoms[5-6]. The peach allergen Pru p 7 is a marker for severe fruit-induced allergy and might be a link between severe allergic reactions to fruits and Cupressaceae (cypress) pollen allergy.[7,8] Pru p 7 is a Gibberellin-regulated protein (GRP), another stable allergen, and homologous, IgE cross-reactive proteins exist in several fruits. Proven Pru p 7 cross-reactivities include the GRP allergens Pru m 7 (Japanese apricot),[9] Cit s 7 (orange)10 and Pun g 7 (pomegranate).[11] Testing of specific IgE (sIgE) to Pru p 7 may be especially useful to fill the gap in diagnosing patients who are peach-allergic but are not sensitized to the other peach allergens Pru p 1 (PR-10), Pru p 3 (LTP) and Pru p 4 (profilin).

Pru p 1 (PR-10) is found in skin and pulp and mainly give local Oral Allergy Syndrome[1]. PR-10s cross-react extensively with Bet v 1 homologues in other fruits and also to a lower degree, PR-10 proteins in legumes such as soy and peanut, and vegetables such as celery and carrot[1].

Available ImmunoCAP Allergen Products*

Stone Fruit Whole allergen – e.g. Apple (f49), Apricot (f237), Peach (f95), Pear (f94), Plum (f255), Almond (f20), Raspberry (f343), Strawberry (f44)

Component		Code
rPru p 1	PR-10	f419
rPru p 3	nsLTP	f420
rPru p 4	Profilin	f421
rPru p 7	GRP	f454
rMal d 1	PR-10	f434
rMal d 3	nsLTP	f435

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactions.

Interpreting the results

Stone fruit allergen	Pru p 1/Mal d 1	Pru p 3/Mal d 3	Pru p 4	Pru p 7	Interpretation
+/-	+				Probability is low for systemic reactions and local symptoms such as OAS are more likely. The patient may be sensitised and reacting to other PR-10-containing pollens and plant foods due to cross- reactions[1,4,12]
+/-		+			Mixed allergy is possible, including systemic and local symptoms such as OAS. The patient may be sensitized and reacting to other nsLTPs contained in other plant foods/ pollens due to cross-reactions which can cause systemic symptoms to both cooked and uncooked foods[1,3-6,12]
+/-			+		Low probability for severe reactions, highly cross-reactive. Positive results can explain broad sensitizations to other plant allergens that contain profilin, including latex, banana, tomato, potato, avocado, timothy grass, peanut etc[1,12]
+/-				+	High risk of systemic reactions, especially in areas with high cypress pollen exposure.[7] The patient may be sensitized and reacting to other GRPs contained in other fruits due to cross-reactions[9-11] which can cause systemic symptoms to both cooked and uncooked fruit.[13]

For other sources of common plant allergen cross-reactions also consider CCD.

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.
2. Faber A et al. IgE-reactivity profiles to nonspecific lipid transfer proteins in a north western European country. J Allergy Clin Immunol. 2017;139(2):679–682.
3. Mothes-Luksch N et al . Pru p 3, a marker allergen for lipid transfer protein sensitization also in Central Europe. Allergy. 2017;72:1415–1418.
4. Sastre J. Molecular diagnosis in allergy. Clinical and Experimental Allergy 2010; 40:1442-1460.
5. Scala E et al. Lipid transfer protein sensitization: reactivity profiles and clinical risk assessment in an Italian cohort. Allergy 70 (2015) 933–943.
6. Pastorello EA et al. Pru p 3-sensitised Italian peach-allergic patients are less likely to develop severe symptoms when also presenting IgE antibodies to Pru p 1 and Pru p 4. Int Arch Allergy Immunol 2011;156:362–372.
7. Klingebiel, C., et al. (2019). Pru p 7 sensitization is a predominant cause of severe, cypress pollen-associated peach allergy. Clin Exp Allergy 49(4): 526-536.
8. Ehrenberg AE, et al. (2020). Characterization of a 7 kDa pollen allergen belonging to the gibberellin-regulated protein family from three Cupressaceae species. Clin Exp Allergy https://doi.org/10.1111/cea.13675.
9. nomata, N., et al. (2017). High prevalence of sensitization to gibberellin-regulated protein (peamaclein) in fruit allergies with negative immunoglobulin E reactivity to Bet v 1 homologs and profilin: Clinical pattern, causative fruits and cofactor effect of gibberellin-regulated protein allergy. J Dermatol 44(7): 735-741.
10. Inomata, N., et al. (2018). Identification of gibberellin-regulated protein as a new allergen in orange allergy. Clin Exp Allergy 48(11): 1509-1520.
11. Tuppo, L., et al. (2017). Pomegranate Cultivars: Identification of the New IgE-Binding Protein Pommaclein and Analysis of Antioxidant Variability. J Agric Food Chem 65(13): 2702-2710.
12. 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.
13. Tuppo, L., et al. (2013). Peamaclein--a new peach allergenic protein: similarities, differences and misleading features compared to Pru p 3. Clin Exp Allergy 43(1): 128-140.

Wheat

Triticum aestivum (Tri a)

Wheat is one of the five most common foods that trigger allergic reactions in children. In Germany, Japan, and Finland it has been reported as the third most common allergen, after milk and egg[1]. The WHO IUIS allergen list now includes 27 wheat allergens[1].

Wheat contains several allergens such as profilin and CCD, which causes wheat extract tests to be positive due to cross-reactions[2]. As wheat is a grass, it cross-reacts with grass pollen[3-4], and with other cereals since many also belong to the grass family[3-5]. Most wheat allergic patients have IgE antibodies to multiple components[5].

Gliadins are non-water soluble proteins but are readily dissolved by stomach acid and are considered as true food allergens. IgE antibodies to gliadin (containing a mix of 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[6-17]. 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)[7-13]. Moreover, ω-5 gliadin has been shown to be a specific risk marker in children with immediate allergy to ingested wheat[14-17].

Available ImmunoCAP Allergen Products*

Wheat – Whole allergen – f4

Component		Code
Gliadin	mix of α, γ, β and ω gliadins	f98
rTri a 19	ω-5 gliadin	f416
rTri a 14	nsLTP	f433

*Complete product names on page 79.

Clinical relevance

Increasing diagnostic specificity, understanding patient risk, indicators of immediate wheat allergy and of wheat-dependent exercise-induced anaphylaxis (WDEIA).

Interpreting the results

f4	f98 gliadin	Tri a 14	Tri a 19	Interpretation
+/-	+			Indicates immediate wheat food allergy with the patient at high risk of severe, systemic reactions and of WDEIA[3,8-18]
+/-		+		Systemic and local symptoms such as OAS are possible. The patient may be sensitised to other nsLTPs contained in other plant foods/pollens due to cross-reactions which can cause systemic symptoms to both cooked and uncooked foods[3,18]
+/-			+	ω-5 gliadin* (omega-5) gives even higher specificity than gliadin f98 and is associated with immediate wheat allergy and WDEIA[3,8-18]

**ω-5gliadin has a natural limited presence on the ImmunoCAP Allergen f4, wheat and some wheat allergic patients, especially WDEIA patients, are negative to the f4-test but positive to ω-5 gliadin*

For other sources of common plant allergen cross-reactions also consider CCD and profilins.

References

1. Czaja-Bulsa et al. What Do We Know Now about IgE-Mediated Wheat Allergy in Children? Nutrients 2017;9(1):35.
2. Matricardi PM et al. Primary versus secondary immunoglobulin E sensitization to soy and wheat inthe Multi-Centre Allergy Study cohort. Clin Exp Allergy. 2008;38(3):493-500.
3. 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
4. Jones SM et al. Immunologic cross-reactivity among cereal grains and grasses in children with food hypersensitivity. J Allergy Clin Immunol.1995 Sep;96(3):341–51.
5. Tatham AS. Shewry PR. Allergens to wheat and related cereals. Clin Exp Allergy 2008; 38:1712-1726.
6. Tanabe S et al. A major wheat allergen has a Gln-Gln-Gln-Pro-Pro motif identified as an IgE-binding epitope. Biochem Biophys Res Commun 1996;219(2):290-293.
7. Battais F et al. Food allergy to wheat: identification of immunogloglin E and immunoglobulin G-binding proteins with sequential extracts and purified proteins from wheat flour. Clin Exp Allergy 2003;33(7):962-970.
8. Park HJ et al. Diagnostic Value of the Serum-Specific IgE Ratio of omega-5 Gliadin to Wheat in Adult Patients with Wheat -Induced Anaphylaxis. Int Arch Allergy Immunol. 2012;157(2)):147-50.
9. Morita E et al. Fast omega gliadin is a major allergen in wheat-dependent exercise- induced anaphylaxis. J Dermatol Sci 2003;33(2):99-104.
10. Palosuo K, et al. Rye gamma-70 and gamma-35 secalins and barley gamma-3 hordein cross-react with omega-5 gliadin, a major allergen in wheat-dependent, exercise-induced anaphylaxis. Clin Exp Allergy 2001;31(3):466-473.
11. Matsuo H et al. Identification of the IgE-binding epitope in omega-5 gliadin, a major allergen in wheat-dependent exercise-induced anaphylaxis. J Biol Chem 2004;279(13):12135 -12140.
12. Palosuo K, et al. A novel wheat gliadin as a cause of exercise-induced anaphylaxis. J Allergy Clin Immunol 1999;103(5,1):912-917.
13. Hofmann SC, et al. IgE detection to αgE detection and its clinical relevance in wheat-dependant exercise-induced anaphylaxis. Allergy 2012;67:1457-1460.
14. Palosuo K, et al. Wheat omega-5 gliadin is a major allergen in children with immediate allergy to ingested wheat. J Allergy Clin Immunol 2001;108(4):634-638.
15. Makela et al. Wheat allergy in children - new tools for diagnostics. Clin Exp Allergy 2014;44:1420-1430.
16. Ito K et al. IgE antibodies to ω-5 gliadin associate with immediate symptoms on oral wheat challenge in Japanese children. Allergy 2008;63:1536-1542.
17. Nilsson N et al. Wheat allergy in children evaluated with challenge and IgE antibodies to wheat components. Pediatr Allergy Immunol 2015;26:119-125.
18. 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

Food allergens from animal sources

Hen's egg

Gallus domesticus (Gal d)

Hen's egg allergy affects up to 2.5% of young children and is potentially life-threatening[1]. 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[2-3]. The use of egg white components is clinically helpful for a fine tuned approach to diagnosis of egg allergy[3]. In particular to help answer the following questions: a) Distinguishing between sensitization and clinical allergy; b) allergy to raw or partially cooked eggs c) allergy to all forms of egg (raw and cooked[3]. Ovomucoid (Gal d 1) has been identified to be the major egg allergen, making up 10% of the egg white protein. Gal d 1 has several important characteristics which makes it more allergenic, such as its stability to cooking and digestion by proteases. Patients with elevated IgE to ovomucoid are at risk for allergic reactions to both raw and cooked egg products[3-8]. Specific IgE to Gal d 1 is also a risk factor for persistent hen's egg allergy[3,9-11]. Over time, egg tolerance is associated with a decrease in IgE to egg white and to ovomucoid[12]. In a recent Danish longitudinal study all positive re-challenge cases correlated with an increase in IgE to ovomucoid[12].

Egg yolk also contains specific allergens such as Livetin/Chicken Serum Albumin (Gal d 5) and YGP42 (Gal d 6)[13-14]. Egg yolk may be somewhat less allergenic than egg white[15] but sensitization to Gal d 5 in egg yolk is related to the bird/egg syndrome[16]. The allergen component Gal d 5 is available on ImmunoCAP ISAC.

Available ImmunoCAP Allergen Products*

Egg white – Whole allergen – f1
Egg yolk – Whole allergen – f75

Component		Code
nGal d 1	ovomucoid	f233
nGal d 2	ovalbumin	f232
nGal d 3	conalbumin	f323
nGal d 4	lysozyme	k208

*Complete product names on page 79.

Clinical relevance

Clinically helpful for distinguishing between allergy to cooked and raw egg, or exclusively to raw egg.

Interpreting the results

f1	Gal d 1	Gal d 2	Gal d 3	Gal d 4	Interpretation
+/-	+				High probability of a persistent egg allergy, patient is at high risk to react both to raw and cooked egg[3-12,17]
+/-		+			Indicates a risk to react to raw egg and a probability to have tolerance to extensively heated egg, especially if Gal d 1 is negative or at low levels[3,7,11-12,17]
+/-			+		
+/-				+	

References

1. Chokshi NY et al. Molecular diagnosis of egg allergy: an update. Expert Rev Mol Diagn. 2015;15(7):895-906
2. Aabin B et al. Identification of IgE-binding egg white proteins: comparison of results obtained by different methods. Int Arch Allergy Immunol 1996;109(1):50-57.
3. 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.
4. Ando H, et al. Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. J Allergy Clin Immunol 2008;122:583-588.
5. Lemon-Mulé H et al. Immunological changes in children with egg allergy ingesting extensively heated egg. J Allergy and Clin Immunol 2008;122;977-983.
6. Urisu A. Allergenic activity of heated and ovomucoid-depleted egg white. J Allergy Clin Immunol 1997;100:171-176.
7. Benhamou Senouf AH et al. Native and denatured egg white protein IgE tests discriminate hen's egg allergic from egg-tolerant children. Pediatr Allergy Immunol 2015;26:12–17.
8. Gray CL et al. Egg sensitization, allergy and component patterns in African children with atopic dermatitis. Pediatr Allergy Immunol 2016;27:709-15.
9. Bernhisel-Broadbent J et al. Allergenicity and antigenicity of chicken egg ovomucoid (Gal d 1)compared with ovalbumin (Gal d 2) in children with egg allergy and in mice. J Allergy Clin Immunol 1994;93;1047-1059.
10. Jarvinen KM et al. Specificity of IgE antibodies to sequential epitopes of hen's egg ovomucoid as a marker for persistence of egg allergy. Allergy 2007; 62:758-765.
11. Benhamou AH et al. State of the art and new horizons in the diagnosis and management of egg allergy. Allergy 2010; 65: 283-289.
12. Gradman J et al. Relationship between specific IgE to egg components and natural history of egg allergy in Danish children. Pediatr Allergy Immunol. 2016 Dec;27(8):825-830.
13. Dhanapala P et al. Cracking the egg: An insight into egg hypersensitivity. Mol Immunol.2015;66(2):375-83.
14. De Silva C et al. Molecular and immunological analysis of hen's egg yolk allergens with a focus on YGP42 (Gal d 6). Mol Immunol. 2016; 71: 152-60.
15. Yanagida N et al. Safety and feasibility of heated egg yolk challenge for children with egg allergies. Pediatr Allergy Immunol. 2017;28(4):348-354.
16. Hemmer W et al. Update on the bird-egg syndrome and genuine poultry meat allergy. Allergo J Int. 2016;25: 68-75.
17. 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.

Cow's milk

Bos domesticus (Bos d)

Milk allergic individuals are often sensitized to more than one milk component and demonstrate varied sensitization profiles[1]. The major allergens in cow's milk are casein, α-lactalbumin and β-lactoglobulin, although other allergens including Bovine Serum Albumin (BSA) and lactoferrin, are also important since 35-50% of patients are sensitized to these allergens[2].

Casein makes up 80% of milk proteins and has been characterized to be thermo-stable[3-4] and resistant to digestion[5]. IgE to casein therefore indicates a risk of allergic reactions to all types of milk products including those that are cooked[6-12]. Milk components have shown to be useful in diagnosing tolerance to extensively heated milk proteins in baked foods. Children with cow's milk allergy (CMA) who have high levels of casein IgE are less likely to tolerate baked milk compared to children with low levels of casein IgE[10-13]. Children with persistant milk allergy have demonstrated to predominantly generate IgE antibodies towards casein[12,14-16]. Furthermore a broader allergen component diversity of IgE and IgG4 binding have been found in children with persistent CMA[17].

A recent study showed patients with a specific type of gastroinestinal cow's milk allergy often have specific IgE against β-lactoglobulin, an important allergen in this particular disease[18].

Bovine Serum Albumin (BSA) is a minor allergen in milk and a major allergen in beef, therefore milk allergic patients sensitised to Bos d 6 (BSA) may have concomitant beef allergy[19-20]. It has also been seen to cross-react with other serum albumins such as pork and sheep[19-20].

Available ImmunoCAP Allergen Products*

Milk – Whole allergen – f2

Component		Code
nBos d 4	α-lactalbumin	f76
nBos d 5	β-lactoglobulin	f77
nBos d 6	BSA	e204
nBos d 8	Casein	f78

*Complete product names on page 79.

Clinical relevance

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

Interpreting the results

f2	Bos d 4	Bos d 5	Bos d 6	Bos d 8	Interpretation
+/-	+				Indicates a risk to react to raw milk and a probability to have tolerance to cooked/baked milk, especially if Bos d 8 is negative or at low levels[1,10-13,21]
+/-		+			
+/-			+		
+/-				+	High probability of a persistent milk allergy, patient is at high risk to have reactions to both raw and cooked milk[1,3-17,21]

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.
2. Kaiser C et al. Cow's milk-protein allergy: results of skin-prick test with purified milk proteins. Z Emahrungswiss 1990;29:122-128.
3. Werfel T et al. Milk-responsive atopic dermatitis is associated with a casein-specific lymphocyte response in adolescent and adult patients. J Allergy Clin Immunol 1997;99 (1):124-133.
4. Norgaard A et al. Allergenicity of individual cow milk proteins in DBPCFC-positive milk allergic adults. J Allergy Clin Immunol 1996,97:237.
5. Dupont D et al. Food processing increases casein resistance to simulated infant digestion. Mol Nutr Food Res 2010;54(11):1677-1689.
6. Docena G, et al. Identification of casein as the major allergenic and antigenic protein of cow's milk. Allergy 1996;51(6):412–416.
7. Shek LP. Humoral and cellular responses to cow milk proteins in patients with milk- induced IgE-mediated and non-IgE mediated disorders. Allergy 2005;60(7):912-919.
8. Lam HY. Cow's milk allergy in adults is rare but severe; both casein and whey proteins are involved. Clin Exp Allergy 2008;38(6):995-1002.
9. Bloom A et al. Effect of heat treatment on milk and egg proteins allergenicity. Pediatric Allergy and Immunology 2015;25:740–746.
10. Nowak-Wegrzyn AK, et al. Tolerance to extensively heating milk in children with cow's milk allergy. J Allergy Clin Immunol 2008;122(2);342-347.
11. Caubet, JC et al. Utility of casein-specific IgE levels in predicting reactivity to baked milk. J Allergy Clin Immunol 2012;131:222-224.
12. Ito K et al. The usefulness of casein-specific IgE and IgG4 antibodies in cow's milk allergic children. Clin Mol Allergy 2012 Jan 2;10(1):1. doi: 10.1186/1476-7961-10-1.
13. Bartuzi Z et al. Contribution of Molecular Allergen Analysis in Diagnosis of Milk Allergy.Curr Allergy Asthma Rep. 2017;17(7):46.
14. Chatchatee P et al. Identification of IgE and IgG binding epitopes on beta- and kappa-casein in cows milk allergic patients. Clin Exp Allergy 2001;31:1256-62.
15. Chatchatee P et al. Identification of IgE- and IgG-binding epitopes on alpha (s1)-casein: differences in patientswith persistent and transient cow's milk allergy. J Allergy Clin Immunol 2001;107:379-83.
16. Cerecedo I et al. Mapping of the IgE and IgG4 sequential epitopes of milk allergens with a peptide microarray-based immunoassay. J Allergy Clin Immunol 2008;122:589-594.
17. Caubet JC et al. Natural tolerance development in cow's milk allergic children: IgE and IgG4 epitope binding. Allergy. 2017 Mar 27. doi: 10.1111/all.13167. [Epub ahead of print]
18. Poza-Guedes P. Role of specific IgE to β-lactoglobulin in the gastrointestinal phenotype of cow's milk allergy. Allergy Asthma Clin Immunol. 2016 Feb 23;12:7.
19. Werfel SJ. Clinical reactivity to beef in children allergic to cow's milk. J Allergy Clin Immunol 1997 99(3):293-300.
20. Martelli A, et al. Beef allergy in children with cow's milk allergy; cow's milk allergy in children with beef allergy. Ann Allergy Asthma Immunol 2002;89(6):Suppl1:38-43.
21. 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.

Red meat

Galactose-alpha-1, 3-Galactose (alpha-gal)

Recently a previously unrecognized clinical syndrome has been reported where systemic reactions occur several (often 3-6) hours after the ingestion of mammalian red meat (beef, pork, lamb and offal, e.g. kidney). The most common symptoms include gastrointestinal problems, urticaria and anaphylaxis[1-13]. Co-factors, such as physical exercise or alcohol potentiate symptoms[5,7-8].

A carbohydrate, the oligosaccharide Galactose-alpha-1, 3-Galactose (alpha-gal), appears to be the allergen causing the reactions[1-6,10,14]. Alpha-gal is present in many mammalian proteins including beef, pork and lamb[7-9]. Measuring specific IgE to alpha-gal is a tool that can be used to support the diagnosis of this type of red meat allergy, which seems to mainly be induced by sensitization by tick bites[10-13], although alpha gal exposure has been reported via the monoclonal antibody cetuximab, which contains the α-Gal epitope on its Fab fragment. Severe reactions to cetuximab infusions have been reported in patients with IgE to α-Gal[14].

Gelatin which is an ingredient in some candies and drugs also contains α-Gal and α-Gal related reactions due to gelatin have been reported[15].

Available ImmunoCAP Allergen Products*

Beef – Whole allergen – f27
Pork – Whole allergen – f26
Mutton – Whole allergen – f88
Gelatin, bovine – Whole allergen – c74

Component		Code
nGal-alpha-1, 3-Gal (alpha- gal)	Thyroglobulin, bovine	o215

*Complete product names on page 79.

Clinical relevance

Alpha-gal can be used as an aid to help confirm alpha-gal related red meat allergy.

Interpreting the results

f27 beef	f26 pork	f88 mutton	c74 gelatin	o215 Alpha-Gal	Interpretation
+/-	+/-	+/-	+/-	+	Suspected cases of α-Gal related allergy is supported by a history of tick bites, delayed symptoms and IgE positivity to several red meats as well as IgE to α-Gal[1-17]

References

1. Commins SP et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose-alpha-1,3-galactose. J Allergy Clin Immunol. 2009 Feb;123 (2):426-33.
2. Saleh H et al. Anaphylactic Reactions to Oligosaccharides in Red Meat: a Syndrome in Evolution. Clinical and Molecular Allergy 2012;10(1):5.
3. Kennedy JL et al. Galactose-alpha-1,3-galactose and delayed anaphylaxis, angioedema, and urticaria in children. Pediatrics 2013;131:e1545-52.
4. Commins SP et al. Delayed clinical and ex vivo response to mammalian meat in patients with IgE to galactose-alpha-1, 3-galactose. J Allergy Clin Immunol. 2014 Jul;134(1):108-15.
5. Caponetto P et al. Gelatin-containing sweets can elicit anaphylaxis in a patient with sensitization to galactose-alpha-1,3-galactose. J Allergy Clin Immunol Pract. 2013 May-Jun;1 (3):302-3.
6. Rispens T et al. IgE production to alpha-gal is accompanied by elevated levels of specific IgG1 antibodies and low amounts of IgE to blood group B. PLoS One. 2013;8(2):e55566.
7. Morisset M et al. Anaphylaxis to pork kidney is related to IgE antibodies specific for galactosealpha-1, 3-galactose. Allergy. 2012;67(5):699-704.
8. Fischer j et al. Galactose-alpha-1,3-galactose sensitization is a prerequisite for pork-kidney allergy and cofactor-related mammalian meat anaphylaxis. J Allergy Clin Immunol 2014;134:755-759.
9. van Nunen S. Galactose-alpha-1, 3-galactose, mammalian meat and anaphylaxis: a worldwide phenomenon? Curr Treat Options Allergy. 2014;1(3):262-77.
10. van Nunen SA et al. An association between tick bite reactions and red meat allergy in humans. Med J Aust. 2009 May 4;190(9):510-1.
11. Hamsten C et al. Identification of galactose-alpha-1,3-galactose in the gastrointestinal tract of the tick Ixodes ricinus; possible with red meat allergy. Allergy 2013;68(4):549-52.
12. Hamsten C et al. Red meat allergy in Sweden: association with tick sensitization and B-negative blood groups. J Allergy Clin Immunol. 2013 Dec;132(6):1431-4.
13. Villalta D et al. Galactose-alpha-1,3-galactose syndrome: an Italian survey. Eur Ann Allergy Clin Immunol. 2017;49(6):263-269.
14. Chung CH et al. Cetuximab-induced anaphylaxis and IgE specific for galactose-α-1,3-galactose. NEJM 2008;358 (11):1109-17.
15. Mullins RJ et al. Relationship between red meat allergy and sensitization to gelatin and galactose-α-1,3-galactose. J Allergy Clin Immunol. 2012 May;129(5):1334-1342.
16. 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.
17. 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.

Shellfish and crustaceans

Shrimp – *Penaeus aztecus* (Pen a)

Shellfish and particularly prawns make up one of the major allergen food groups[1-2]. Tropomyosin (Pen a 1, Pen m 1) is considered a major allergen in shrimp and crustacean allergy[3]. Arginine kinase (Pen m 2), myosin light chain and sarcoplasmic calcium binding protein (Pen m 4) have been identified as minor crustacean allergens[4-7]. Pen m 2 and Pen m 4 are available on ImmunoCAP ISAC.

60% of individuals with confirmed allergy to shellfish produce specific IgE which binds to tropomyosin[8]. Due to its wide-spread occurrence, tropomyosin can be both inhaled and ingested. Pen a 1 as well as Pen m 1 is heat stable, causing reactions both to raw and cooked shrimp[9]. Tropomyosin proteins (Pen a 1, Pen m 1), are highly cross-reactive amongst many invertebrate species such as shrimps other crustacean foods such as crab, lobster snail and molluscs as well as dust mites (Der p 10), cockroaches (Bla g 7) and helminths[10].

Prevalence of dust mite-allergic patients with IgE to tropomyosin is reportedly between 5-18%[6]. Some studies suggested that dust mite immunotherapy or respiratory exposure to dust mite tropomyosin may induce tropomyosin sensitization causing food allergy to shrimps[11]. Patients with IgE to Der p 10 may potentially have a higher probabiity of allergic reactions to shellfish (crustaceans and mollusc), insects and parasites[11].

Available ImmunoCAP Allergen Products*

Shrimp – Whole allergen – f24
Crab – Whole allergen – f23
Blue mussel – Whole allergen – f37

Component		Code
rPen a 1	Tropmyosin	f351
rDer p 10	Tropomyosin	d205

*Complete product names on page 79.

Clinical relevance

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

f24/ f23	Pen a 1	Der p 10	Interpretation
+/-	+		Probability to react to different tropomyosins and to crustacean foods in general – cross-reactions through tropomyosin can cause systemic symptoms[3,8-12]
+/-		+	Some patients sensitised to Der p 10 may react to crustacean tropomyosin such as Pen a 1 in shrimp. These patients are at higher probability of crustacean allergy[6,8,10-12]

References

1. Leung NYH, et al. Current immunological and molecular biological perspectives on seafood allergy: A comprehensive review. Clin Rev Allergy Immunol. 2014;;46(3):180-97.
2. Mariona P et al. Molecular Diagnosis of Shrimp Allergy: Efficiency of Several Allergens to Predict Clinical Reactivity Journal of Allergy and Clinical Immunol: In Practice 2015;3(4):521-529.
3. Shanti KN et al. Identification of tropomyosin as the major shrimp allergen and characterization of its IgE-binding epitopes. J Immunol 1993;151(10):5354-5363.
4. Yu CJ et al. Proteomics and immunological analysis of a novel shrimp allergen, Pen m 2. J Immunol 2003;170:445-453.
5. Ayuso R et al. Myosin light chain is a novel shrimp allergen, Lit v 3. J Allergy Clin Immunol 2008;122:795-802.
6. Shiomi K et al. Sarcoplasmic calcium-binding protein: identification as a new allergen of the black tiger shrimp Penaeus monodon. Int Arch Allergy Immunol 2008;146:91-98.
7. Giuffrida MG et al. Shrimp allergy beyond Tropomyosin in Italy: clinical relevance of Arginine Kinase, Sarcoplasmic calcium binding protein and Hemocyanin. Eur Ann Allergy Clin Immunol. 2014 46;(5):172-177.
8. 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.
9. Lopata AL and Lehrer SB. New insights into seafood allergy. Curr Opin Allergy Clin Immunol 2009;9:270-277.
10. DeWitt AM et al. Recombinant tropomyosin from Penaeus aztecus (rPen a 1) for measurement of specific immunoglobulin E antibodies relevant in food allergy to crustaceans and other invertebrates. Mol Nutr Food Res 2004;48(5):370-379.
11. Fernandes J. Immunoglobulin E antibody reactivity to the major shrimp allergen, tropomyosin, in unexposed Orthodox Jews. Clin Exp Allergy 2003;33:956.
12. 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.

Fish Allergens

Cod – *Gadus callarius* (Gad c), Carp – *Cyprinus carpio* (Cyp c)

Increases in global fish consumption have led to rise in the reports of fish related allergy[1]. The route of exposure is not just restricted to ingestion but also manual handling and inhalation which are important factors for consideration in occupational exposure[1].

Parvalbumins are major allergens in fish (and amphibians such as frogs)[1-8]. This protein allergen group causes a major clinical cross reactivity between fish species, resulting in over 90% of fish allergic patients reacting to almost all fish species[1-4,7-8]. Fish parvalbumin is a highly stable molecule[8] and is resistant to cooking and digestion. Recombinant carp parvalbumin (rCyp c 1) was found to contain 70% of the IgE epitopes present in natural extract of cod, tuna and salmon[2]. This suggested that carp parvalbumin would make a valid tool in the diagnosis of patients with fish allergy[2].

Parvalbumins are expressed in lower levels in certain fish species such as tuna, swordfish and some mackerels. This perhaps explains why some fish-allergic patients can tolerate these species[1,6,9].

Available ImmunoCAP Allergen Products*

Fish whole allergen – e.g. Cod (f3) Haddock (f42), Salmon (f41), Mackerel (f206)

Component		Code
rGad c 1	Parvalbumin	f426
rCyp c 1	Parvalbumin	f355

*Complete product names on page 79.

Clinical relevance

Understanding risk and cross-reactive determinations.

Interpreting the results

f3	Gad c 1	Cyp c 1	Interpretation
+/-	+		Primary allergen in fish, high probability of allergy to cod and closely related fish (white fish but also other fishes) due to cross-reactions[1-10]
+/-		+	High probability of allergy to carp and closely related fish (oily fish) due to cross-reactions[1-10]

References

1. Sharp MF et al. Fish allergy: in review. Clin Rev Allergy Immunol 2014;46:258-271.
2. Swoboda I, et al. Recombinant carp parvalbumin, the major cross-reactive fish allergen: a tool for diagnosis and therapy of fish allergy. Allergy 2002; 57: Suppl 73:79-84.
3. Bugajska-Schretter A et al. Parvalbumin, across-reactive fish allergen, contains IgE-binding epitopes sensitive to periodate treatment and Ca2+ depletion. J Allergy Clin Immunol 1998 101:67–74.
4. Lim DL-C et al. Parvalbumin- the major tropical fish allergen. Pediatr Allergy Immunol 2008 19:399–407.
5. Bugajska-Schretter A et al. Purification, biochemical, and immunological characterisation of a major food allergen: different immunoglobulin E recognition of the apo- and calcium-bound forms of carp parvalbumin. Gut 2000;46(5):661-669.
6. Griesmeier U et al. Expression levels of parvalbumins determine allergenicity of fish species. Allergy 2010;65:191-198.
7. Kuehn A et al. Identification of enolases and aldolases as important fish allergens in cod, salmon and tuna: component resolved diagnosis using parvalbumin and the new allergens. Clin Exp Allergy 2013;43:811-822.
8. 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.
9. Kuehn A. Fish Allergens at a Glance: Variable Allergenicity of Parvalbumins, the Major Fish Allergens. Front Immunol. 2014;5:179.
10. 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

Inhalant allergen components

Inhalant sensitization to aeroallergens such as dust mite, animal dander and pollen can cause allergy in two ways. Initially causing primary allergy, often linked to respiratory symptoms. Furthermore pollen sensitized individuals also can suffer from secondary cross-reactions, which can result in local symptoms such as Pollen-Food Syndrome[1].

Revealing the primary allergen source driving the allergy could help improve allergy management such as exposure reduction strategies[2-3] 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 containing the right allergens administered[4-6].

Immunotherapy vaccins vary in their composition of molecular allergens, for example birch immunotherapy vaccines contain mainly the birch major allergen Bet v 1 (PR-10). Quantities of allergen present vary from manufacturer to manufacturer[7-11]. Allergen extracts may be reflective of how much of the allergen is present at the source. The levels of Der p 23 in mite faecal particles and bodies is rather low[12].

References

1. Popescu FD. Cross-reactivity between aeroallergens and food allergens. World J Methodol 2015 June 26;5(2):31-50.
2. Murray S et al. Preventing severe asthma exacerbations in children: A randomised trial of mite impermeable bedcovers. Am J Respir Crit Care Med. 2017 Jul 15;196(2):150-158.
3. Morgan JW et al. Results of Home based Environment Intervention among Urban Children with Asthma. N Engl J Med 2004;351:1068-1080.

4. Canonica GW et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
5. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
6. Schmid-Grendelmeier P et al. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953.
7. Focke M et al. Heterogeneity of commercial timothy grass pollen extracts. Clin Exp Allergy 2008;38(8):1400-1408.
8. Focke M et al. Molecular composition and biological activity of commercial birch pollen allergen extracts. Eur J Clin Invest 2009;39(5):429-436.
9. Brunetto B et.al Characterization and comparison of commercially available mite extracts for in vivo diagnosis. Allergy 2010;65(2):184-90.
10. Casset A et al. Varying allergen composition and content affects the in vivo allergenic activity of commercial Dermatophagoides pteronyssinus extracts. Int Arch Allergy Immunol. 2012;159(3):253-62.
11. Moreno Benitez F et al. Variation in allergen content in sublingual allergen immunotherapy with house dust mites. Allergy. 2015;70(11):1413-20.
12. Weghofer M et al. Identification of Der p 23, a peritrophin-like protein, as a new major Dermatophagoides pteronyssinus allergen associated with the peritrophic matrix of mite fecal pellets. J Immunol. 2013;190(7):3059-67.

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.

Clinically uteroglobin and lipocalins have been identified as the most important major allergen components from cat, dog and horse[1-3]. Serum albumins are often considered to have less clinical relevance in allergy to furry animals, they are minor allergens that cause multiple positivity due to crossreactivity when using extract tests. However serum albumins are important food allergens in meat[4].

References

1. Hilger C et al. Animal Lipocalin allergens. Curr Allergy Asthma Rep 2012;12 438 – 447.
2. Nordlund B et al. IgE antibodies to animal-derived lipocalin, kallikrein and secretoglobin are markers of bronchial inflammation in severe childhood asthma. Allergy 2012:67:661–9.
3. Konradsen JR et al. Allergy to Furry animals: New Insights, diagnostic approaches, and challenges. J Allergy Clin Immunol 2015;135:616-25.
4. Werfel SJ. Clinical reactivity to beef in children allergic to cow's milk. J Allergy Clin Immunol 1997;99(3):293-300.

Cat

Felis domesticus (Fel d)

Sensitization to cat is strongly associated with asthma, especially in environments free of mite and cockroach[1-2]. Children with cat allergy and problematic severe asthma have higher levels of IgE antibodies towards cat compared with children with controlled asthma[3]. Fel d 1 is the major cat allergen, belonging to the uteroglobin family and is produced in the salivary glands and skin. Multiple sensitizations towards lipocalins (Fel d 4, Fel d 7) and uteroglobins (Fel d 1) have been associated with increased bronchial inflammation in severe asthmatics[4-7]. The lipocalin Fel d 7[16,17] is only recently (2018) commercially available, and shows homology to Dog, Can f 1 so cross reactions could be expected[17].

Allergy to cat dander and pork meat, also referred to as the pork/cat syndrome[8-9], has been described to be mediated by cross-reactive IgE antibodies recognizing cat serum albumin (Fel d 2) and pig serum albumin[10].

Available ImmunoCAP Allergen Product*

Cat – Whole allergen – e1

Component		Code
rFel d 1	uteroglobin	e94
rFel d 2	cat serum albumin	e220
rFel d 4	lipocalin	e228
rFel d 7	lipocalin	e231

*Complete product names on page 79.

Clinical relevance

Understanding primary sensitization to cat, aiding immunotherapy selection (see Immunotherapy section) and markers of severity. AIT success is more likely if sensitization to specific components is identified[11-13].

Interpreting the results

e1	Fel d 1	Fel d 2	Fel d 4	Fel d 7	Interpretation
+/-	+				Major allergen. Primary sensitization to Cat. Fel d 1 positive patients are suitable for AIT[4-7,11-15]
+/-		+			Minor allergen. IgE to Fel d 2 (cat serum albumin) can indicate cross reactivity and is seldom of clinical importance in inhalant allergy, however Fel d 2 can be a primary sensitiser in Pork-Cat-Syndrome[8-10,14,15]
+/-			+		Major allergen. Fel d 4 sensitization is associated with severe asthma symptoms in cat allergic patients with Fel d 1 reactivity[4-7,14-15]. Sensitization to Fel d 4 but not Fel d 1 suggests cross-reactivity from other furry animal e.g. dog or horse.
+/-				+	Minor allergen[16] which cross-reacts with dog Can f 1, and the highest sIgE level indicates which is the primary sensitizer.[18]

References

1. Ingram JM et al. Quantitative assessment of exposure to dog (Can f 1) and cat (Fel d 1) allergens: Relation to sensitization and asthma among children living in Los Alamos, New Mexico. J Allergy Clin Immunol 1995;96:449-56.
2. Bjerg A et al. A population-based study of animal component sensitization, asthma, and rhinitis in schoolchildren. Pediatr Allergy Immunol. 2015;26(6):557-63.
3. Konradsen JR et al. Severe childhood asthma and allergy to furry aninmals: Refined assessment and using molecular based allergy diagnostics. Pediatr Allergy Immunol. 2014;25:187 - 192.
4. Nordlund B et al. IgE antibodies to animal-derived lipocalin, kallikrein and secretoglobin are markers of bronchial inflammation in severe childhood asthma. Allergy 2012;67:661-669.

5. Konradsen JR et al. Allergy to Furry animals: New Insights, diagnostic approaches, and challenges. J Allergy Clin Immunol 2015;135:616-25.
6. Nagao M et al. Sensitization to secretoglobin and lipocalins in a group of young children with risk of developing respiratory allergy. Clin Mol Allergy 2017;3;15:4. doi: 10.1186/s12948-017-0061-8. eCollection 2017.
7. Asarnoj A et al. Sensitization to cat and dog allergen molecules in childhood and prediction of symptoms of cat and dog allergy in adolescence: A BAMSE/MeDALL study. J Allergy Clin Immunol. 2016;137(3):813-21.
8. Drouet M and Sabbah A. The Pork/Cat Syndrome or Crossed Reactivity between Cat Epithelia and Pork Meat. Monogr Allergy 1996; 32:164-73.
9. Posthumous J et al. Initial description of pork-cat syndrome in the United States. J Allergy Clin Immunol 2013;131:924–925 (letter to the editor).
10. Hilger C et al. Allergic cross-reactions between cat and pig serum albumin. Allergy 1997;52:179-87.
11. Canonica GW et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
12. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
13. Schmid-Grendelmeier P et al. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953.
14. 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.
15. 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.
16. Smith W, O'Neil SE, Hales BJ, et al. Two newly identified cat allergens: the von Ebner gland protein Fel d 7 and the latherin-like protein Fel d 8. Int Arch Allergy Immunol 2011;156:159-70.
17. Hilger C, Kuehn A, Hentges F. Animal lipocalin allergens. Curr Allergy Asthma Rep 2012;12:438-47.
18. Apostolovic D et al. The cat lipocalin Fel d 7 and its cross-reactivity with the dog lipocalin Can f 1. Allergy. 2016 Oct;71(10):1490-5.

Dog

Canis familiaris (Can f)

Like cat allergy, allergy to dogs is considered to be a major risk factor of the development of asthma and rhinitis[1] and allergy to these animals reduces quality of life[2]. Can f 1, lipocalin is a major dog allergen and a primary sensitizer. It is found in all homes with a dog and up to one third of homes without a dog[3]. Many dog allergics are sensitized to Can f 1 and /or Can f 2, both lipocalin allergens, but prevalence differs in different patient populations[4]. Children with severe asthma in a Swedish study[2] demonstrated sensitization to 3 or more lipolcalins including Can f 2. Other lipocalins identified to be of clinical importance are Can f 4[5] and Can f 6[6]. Can f 3, dog serum albumin is abundant in saliva and dander, and is highly cross reactive with other serum albumins from other species such as Fel d 2 from cat[7]. Serum albumins are generally considered minor allergens[7]. Can f 5 is an important allergen from male dogs and IgE antibodies to Can f 5 can be found in up to 70% of patients with dog allergy in certain populations[8-11].

Available ImmunoCAP Allergen Products*

Dog – Whole allergen – e5

Component		Code
rCan f 1	lipocalin	e101
rCan f 2	lipocalin	e102
nCan f 3	dog serum albumin	e221
rCan f 4	lipocalin	e229
rCan f 5	kallikrein	e226
rCan f 6	lipocalin	e230

*Complete product names on page 79-80.

Clinical relevance

Understanding primary sensitization to dog, aiding immunotherapy selection, markers of severity. AIT success is more likely if sensitization to specific components is identified[12-14].

Interpreting the results

e5	Can f 1	Can f 2	Can f 3	Can f 4	Can f 5	Can f 6	Interpretation
+/-	+						Major allergen. Primary sensitization to dog. Cross-reactivity with cat, Fel d 7[16]. Positive patients are suitable for AIT[2-4,7,12-15]
+/-		+					Important allergen. Primary sensitization to dog. Can f 2 sensitization is associated with severe asthma symptoms[2,4,7,15]. Patients are suitable for AIT[2-4,7,12-15]
+/-			+				Minor allergen. Can f 3 (dog serum albumin) is associated with cross reactivity (e.g. dog or horse) and is seldom of high clinical importance[7,15]
+/-				+			Minor allergen. About one third of dog allergic patients have specific IgE to this allergen[5, 15]
+/-					+		Major allergen. Can f 5 sensitization is associated with male dogs. Mono sensitization may suggest female dogs are suitable pets. May be relevant to human seminal fluid allergy cross-reactions[7, 8-11,15]
+/-						+	Major allergen. Cross-reactive with Equ c 1 (horse) and Fel d 4 (cat) where the highest sIgE level suggest the primary sensitizer.[7,15]

References

1. Perzanowski MS et al. Effect of cat and dog ownership on sensitization and development of asthma among pre-teenage children. Am J Respir Crit Care Med 2002:166:696–702.
2. Nordlund B et al. IgE antibodies to animal-derived lipocalin, kallikrein and secretoglobin are markers of bronchial inflammation in severe childhood asthma. Allergy 2012:67:661–9.
3. Nicholas C et al. Dog characteristics and allergen levels in the home. Ann Allergy Asthma Immunol 2010;105:228-33.
4. Konradsen JR et al. Allergy to Furry animals: New Insights, diagnostic approaches, and challenges. Allergy Clin Immunol 2015;135:616-25.
5. Mattsson L. Molecular and immunological characterization of Can f 4: a dog dander allergen cross-reactive with a 23 kDa odorant-binding protein in cow dander. Clin Exp Allergy 2010; 40(8):1276-1287.
6. Jakob T et al. Clinical relevance of sensitization to cross-reactive lipocalin Can f 6. Allergy 2013;68(5):690-691.
7. 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.
8. Mattsson L et.al. Prostatic kallikrein: A new major dog allergen. J Allergy Clin Immunol 2009; 123(2):362-368.
9. Basagaña M. Involvement of Can f 5 in a Case of Human Seminal Plasma Allergy Int Arch Allergy Immunol 2012;159:143–146.
10. Kofler L. et al. A case of dog-related human seminal plasma allergy Eur Ann Allergy Clin Immunol 2012 Apr;44(2):89-92.
11. Schoos AM et al. Precision allergy: Separate allergies to male and female dogs. J Allergy Clin Immunol Pract. 2017 Nov-Dec;5(6):1754-1756.
12. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
13. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
14. Schmid-Grendelmeier P et al. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953
15. 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.
16. Apostolovic D et al. The cat lipocalin Fel d 7 and its cross-reactivity with the dog lipocalin Can f 1. Allergy. 2016 Oct;71(10):1490-5.

Horse

Equus caballus (Equ c)

Horse allergy occurs among people who handle horses regularly, either professionally or for recreational purposes, and results in the induction or exacerbation of asthma, allergic rhinitis, allergic conjunctivitis and occupational asthma. Horse allergens have potential to cause severe allergic reaction but are often overlooked[1-3]. Up to now two lipocalins have been identified in horse - Equ c 1 and Ecu c 2. Equ c 1 is the major horse allergen and up to 76% of patients with horse allergy react[3-4]. Lipocalins are associated with severe childhood asthma[4-5]. As with other furry animals summarized in this book, horses produce serum albumin allergen (Ecu c 3), which is often referred to as a minor allergen[5-6]. Cross-reactions between patients allergic to horse albumin and other albumins from dog, cat, or guinea pig albumin are common[1]. Horse dander can easily be transferred into homes or public places such as schools by family members to horse riders. Equ c 3 is available on ImmunoCAP ISAC.

Available ImmunoCAP Allergen Products*

Horse – Whole allergen – e3

Component		Code
rEqu c 1	Lipocalin	e227

*Complete product names on page 79.

Clinical relevance

Understanding primary sensitization to horse, aiding immunotherapy selection, markers of severity. AIT success is more likely if sensitization to specific components is identified[6-9].

Interpreting the results

e3	Equ c 1	Interpretation
+/-	+	Major allergen. Primary sensitization to horse. Patients positive to Equ c 1 may be suitable for AIT[3-10]

References

1. Gawlik et al. Anaphylaxis as a manifestation of horse allergy. WAO Journal 2009;2:185–189.
2. Cosme-Blanco W et al Anaphylaxis to Horses and Epinephrine Use: Increasing Awareness Among Pediatric Patients and Families. Pediatr Allergy Immunol 2017;28(6):608-610.
3. Roberts G and Lack G. Horse allergy in children. BMJ. 2000;321: 286 –287.
4. Konradsen JR et al. Allergy to Furry animals: New Insights, diagnostic approaches, and challenges. Allergy Clin Immunol 2015;135:616-25.
5. Nordlund B et al. IgE antibodies to animal-derived lipocalin, kallikrein and secretoglobin are markers of bronchial inflammation in severe childhood asthma. Allergy 2012:67:661–9.
6. 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.
7. Canonica GW et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
8. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
9. Schmid-Grendelmeier P et al. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953.
10. 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.

House dust mites

Dermatophagoides pteronyssinus (Der p)
Dermatophagoides farinae (Der f)

Allergy to house dust mites (HDM) is a main cause of respiratory allergies, and exposure to HDM is a major trigger of asthma exacerbations[1]. *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[2].

Together Der p 1 and Der p 2 will identify between 63 and 97% of patients sensitised to Der p extracts[3]. Thus, a significant proportion (up to 37%) of house dust mite sensitised patients may be missed by the use of only group 1 and group 2 specific IgE component tests.

Der p 23 has recently been identified as another major dust mite allergen present on the surface of mite faecal particles, which is the major airborne form of mite allergens[4]. It is present in low levels in the allergen source[4-6]. Up to 74% of *Dermatophagoides pteronyssinus* allergic patients are sensitized to Der p 23[4-5]. Der p 23 appears highly clinically relevant[7]. Early sensitization in children to either: Der p 1, Der p 2 or Der p 23 is associated with asthma development[8]. Asthma patients are sensitized to more mite allergen components than those without asthma[9]. Sensitization to Der p 1 and Der p 23 before the age of five was predictive of asthma at school-age[9]. Tropomyosin (Der p 10) is the main cross reactive allergen between mites, shellfish, cockroaches and helminths. Therefore in cases where genuine sensitization is unclear specific allergen components can be useful to identify primary allergy[2]. Tropomyosin is a minor allergen in mite allergy but considered a major allergen in shellfish allergy[2].

Available ImmunoCAP Allergen Products*

Dermatophagoides pteronyssinus – Whole allergen – d1
Dermatophagoides farinae – Whole allergen – d2

Component		Code
rDer p 1	(Group 1) Cysteine protease	d202
rDer p 2	(Group 2) NPC2 protein family (epidermal secretory proteins)	d203
rDer p 10	Tropomyosin	d205
rDer p 23	Peritrophin-like protein	d209

*Complete product names on page 79.

Clinical Relevance

Identifying primary allergens when sensitization is not clear. Aiding choice of allergen immunotherapy. AIT success is more likely if sensitization to specific components is identified[10-12].

Interpreting the results

d1 or d2	Der p 1	Der p 2	Der p 10	Der p 23	Interpretation
+/-	+				Major allergen, primary sensitizer. Good indicator for AIT[2-3,5,6,8-14]
+/-		+			Major allergen. Primary sensitizer. May be under represented in AIT potentially leading to reduced efficacy[2-6,8-14]
+/-			+		Minor allergen. Cross reactive to other species including shellfish. 10% prevalence sensitization in children and adults with asthma. May be under represented in AIT potentially leading to reduced efficacy[2,6,14]
+/-				+	Major allergen. Primary sensitizer. Low levels in the natural source[2,4-14]

References

1. Calderon MA et al. House Dust Mite Respiratory Allergy: An Overview of Current Therapeutic Strategies. The journal of allergy and clinical immunology In practice. 2015;3(6):843-55.
2. 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.
3. Nolte H et al. Major allergen content consistency of SQ house dust mite sublingual immunotherapy tablets and relevance across geographic regions. Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology. 2016;117(3):298-303.
4. Weghofer M et al. Identification of Der p 23, a peritrophin-like protein, as a new major Dermatophagoides pteronyssinus allergen associated with the peritrophic matrix of mite fecal pellets. J Immunol. 2013;190(7):3059-67.
5. Becker S et al. Real-Life Study for the Diagnosis of House Dust Mite Allergy - The Value of Recombinant Allergen-Based IgE Serology. Int Arch Allergy Immunol. 2016;170(2):132-7.
6. Casset A et al. Varying allergen composition and content affects the in vivo allergenic activity of commercial Dermatophagoides pteronyssinus extracts. Int Arch Allergy Immunol. 2012;159(3):253-62.
7. Mueller GA et al. Serological, genomic and structural analyses of the major mite allergen Der p 23. Clin Exp Allergy. 2016;46(2):365-76.
8. Posa D et al. Evolution and predictive value of IgE responses toward a comprehensive panel of house dust mite allergens during the first 2 decades of life. J Allergy Clin Immunol 2017;139:541-549.
9. Resch Y et al. Different IgE recognition of mite allergen components in asthmatic and non asthmatic children. The Journal of allergy and clinical immunology. 2015;136(4):1083-91.
10. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
11. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
12. Schmid-Grendelmeier P et al. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953.
13. Thomas WR. House Dust Mite Allergens: New Discoveries and Relevance to the Allergic Patient. Current allergy and asthma reports. 2016;16(9):69.
14. 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.

Pollen – Grasses

Timothy Grass – *Phleum pratense* (Phl p)
Bermuda grass – *Cynodon dactylon* (Cyn d)

Grass pollen allergy is common worldwide, and in some regions up to 40% of atopics show sensitization to grass pollen[1-3]. 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[4]. Group 1 and group 5 allergens (Phl p 1, Cyn d 1 and Phl p 5) are dominating grass pollen allergens and markers of primary sensitization. More than 90% of patients with sensitization to grass pollen have IgE abs to Phl p 1 and/or Phl p 5[2,5-7]. Sensitization to Phl p 1 usually precedes other grass pollen component sensitizations in the development of hay fever symptoms[3].

When no specific grass sensitization is detected in multisensitized patients, other pollen or food specific components should be investigated[2,5,8]. Sensitization to cross-reactive minor allergens such as profilin (Phl p 12) and polcalcin (Phl p 7) is usually not frequent (< 20 %) but sensitization to CCD is rather common and many plant foods contain both profilin and CCD. Sensitization to minor allergens such as Phl p 7 in addition to major components indicates more complex sensitization profiles and has been associated with more severe symptoms and longer duration of disease[7].

Available ImmunoCAP Allergen Products*

Bermuda grass – Whole allergen – g2
Timothy grass – Whole allergen – g6

Component		Code
nCyn d 1	grass group 1, CCD bearing protein	g216
rPhl p 1	grass group 1	g205
rPhl p 2	grass group 2	g206
nPhl p 4	CCD-bearing protein	g208
rPhl p 5b	grass group 5	g215
rPhl p 6	grass group 6	g209
rPhl p 7	Polcalcin	g210
rPhl p 11	Ole 1-related protein	g211
rPhl p 12	Profilin	g212
rPhl p 1	+ rPhl p 5b	g213**
rPhl p 7	+ rPhl p 12	g214**
CCD	MUXF3 from Bromelain	o214

*Complete product names on page 79.

**ImmunoCAP sIgE test with 2 allergen components (available in certain countries/ regions)

Clinical Relevance

Identifying primary grass allergy and utilisation in AIT management[9-14].
Identifying cross-reactivities.

Interpreting the results

g2/g6	Cyn d 1	Phl p 1	Phl p 5b	Phl p 7	Phl p 12	Interpretation
+/-	+					Primary sensitization to Bermuda grass when CCD sensitization is excluded. Good candidate for AIT[1-4, 9-15]
+/-		+				Primary sensitization to Timothy. Phl p 1 and Phl p 5b are major allergens. Good candidate for AIT[1-7,9-15]
+/-			+			
+/-				+		Phl p 7 and Phl p 12 are cross reactive minor allergens which may not be available in sufficient amounts in AIT extract. IgE to Phl p 7 and 12 alone indicate low suitability for grass pollen SIT. The primary allergen should be identified[7-15]
					+	

For other sources of common plant allergen cross-reactions also consider CCD.

References

1. Barber D et al. Understanding patient sensitization profiles in complex pollen areas: a molecular epidemiological study. Allergy. 2008 Nov; 63(11):1550–8.
2. Andersson K et al. Characteristics and immunobiology of grass pollen allergens. International Archives of Allergy & Immunology. 2003;130(2): 87–107.
3. Hatzler L et al. Molecular spreading and predictive value of preclinical IgE response to Phleum pratense in children with hay fever. J Allergy Clin Immunol. 2012 Oct;130(4):894–901 e5.
4. 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.
5. Sekerkova A et al. Detection of Phl p 1, Phl p 5, Phl p 7 and Phl p 12 specific IgE antibodies in the sera of children and adult patients allergic to Phleum pollen. Allergol Int. 2012 Jun; 61(2):339–46.
6. Tripodi S et al. Molecular profiles of IgE to Phleum pratense in children with grass pollen allergy: Implications for specific immunotherapy. J Allergy Clin Immunol. 2012 Mar;129(3): 834–9 e8.
7. Cipriani F et al. Diagnostic relevance of IgE sensitization profiles to eight recombinant Phleum pratense molecules. Allergy 2017;Oct 20. doi: 10.1111/all.13338. [Epub ahead of print].
8. Hauser M et al. Panallergens and their impact on the allergic patient. Allergy Asthma Clin Immunol. 2010;6(1):1.
9. Schmid-Grendelmeier P. Recombinant allergens – routine diagnostics or still only science? Der Hautarzt 2010;61(11):946-953.
10. Focke M et al. (2008) Heterogeneity of commercial timothy grass pollen extracts. Clin Exp Allergy 38(8):1400–1408.
11. Walker SM et al. Immunotherapy for allergic rhinitis. Clin Exp Allergy. 2011 Sep; 41(9): 1177–200.
12. Valenta R. et al. Component-resolved diagnosis to optimize allergen-specific immunotherapy in the Mediterranean area. J Investig Allergol Clin Immunol. 2007;17 Suppl 1:36–40.
13. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
14. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
15. 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.

Pollen – Trees

Birch – *Betula verrucosa* – (Bet v)

Many birch pollen allergic patients are sensitized and react to several pollen, either due to multiple primary sensitizations or due to allergen cross-reactivity[1-3]. Birch is closely related to several other trees such as alder, hazel, beech and oak. In addition, many of these patients have concomitant pollen-related food allergies due to PR-10 cross-reactivity[1,4]. Therefore patients sensitized to Bet v 1 may react to various fruits, nuts and vegetables such as apple, pear or hazelnut[1,4]. In most cases, symptoms to the triggering food are restricted to oral reactions and the food is often tolerated when cooked since PR-10 allergens are heat labile[4-5].

Birch AIT treatment

- Patients sensitized to the specific birch component Bet v 1 are more likely to get symptom relief by birch pollen AIT[6-7]
- Patients sensitized to minor, cross-reactive birch components only, have less successful outcomes of birch pollen AIT[6-7]

Available ImmunoCAP Allergen Products*

Birch – Whole allergen – t3

Component		Code
rBet v 1	PR-10	t215
rBet v 2	Profilin	t216
rBet v 4	Polcalcin	t220
rBet v 6	Isoflavone reductase like	t225
rBet v 2	+ rBet v 4	t221**
CCD	MUXF3 from Bromelain	o214

*Complete product names on page 79.

**ImmunoCAP sIgE test with 2 allergen components (available in certain countries/ regions)

Clinical Relevance

Identifying primary birch allergy and utilisation in AIT management.

Explain birch pollen-related food allergies (Bet v 1, Bet v 2, Bet v 6)[1,4].

Clarify sensitization due to cross-reactivity (Bet v 2, Bet v 4, Bet v 6)[4,8].

Interpreting the results

t3	Bet v 1	Bet v 2	Bet v 4	Bet v 6	Interpretation
+/-	+				Primary sensitization to Birch. Bet v 1 is a major allergen. Good candidate for AIT. In food allergy cases patient may react to various fruits, nuts and vegetables containing PR-10 allergens[1-12]
+/-		+			Bet v 2, Bet v 4 and Bet v 6 are cross-reactive minor allergens which may not be available in sufficient amounts in AIT extract. IgE to Bet v 2 and Bet v 4 alone indicate low suitability for birch pollen AIT. The primary allergen should be identified[1,6-12]
+/-			+		
+/-				+	

For other sources of common plant allergen cross-reactions also consider CCD.

References

1. Hauser M et al. Panallergens and their impact on the allergic patient. Allergy, Asthma & Clinical Immunology. 2010;6(1)1.
2. Rossi RE et al. Sensitization profiles in polysensitised patients from a restricted geographical area: Further lessons from multiplexed component resolved diagnosis. Eur Ann Allergy Clin Immunol. 2011; 43(6):171–175.
3. Hauser M et.al. Bet v 1-like pollen allergens of multiple Fagales species can sensitize atopic individuals. Clinical & Exp Allergy. 2011;41:1804–181.
4. Vieths S et al. Current understanding of cross-reactivity of food allergens in pollen. Ann N.Y Acad Sci. 2002;964:47–68.
5. Schmidt-Andersen MB et al. Identification of European allergy patterns to the allergen families PR-10, LTP and profiling from Rosaceae fruits. Clin Rev Allerg Immunol. 2009; 41(1):4–19.
6. Valenta R et al. Component-Resolved Diagnosis to Optimize Allergen-Specific Immunotherapy in the Mediterranean area. J Invest Allergol Clin Immunol. 2007;Vol 17, supplement 1:88–92.
7. Schmid-Grendelmeier P. Recombinant allergens. For routine use or still only science? Hautarzt. 2010;61(11):946–53.
8. Sekerková A et al. Detection of Bet v 1, Bet v 2 and Bet v 4 specific IgE antibodies in the sera of children and adult patients allergic to birch pollen: evaluation of different IgE reactivity profiles depending on age and local sensitization. Int Arch Allergy Immunol. 2011;154:278–285.
9. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
10. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
11. 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.
12. 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.

Other trees

Olive tree – *Olea europea* – (Ole e)

European Ash – *Fraxinus excelsior* – (Fra e)

Olive and ash are botanically very closely related (*Oleaceae* family) and extensive cross-reactivity between these species occurs[1-4]. Olive fruit allergy is quite rare, whilst olive tree pollen allergy is quite common and is one of the most important causes of seasonal respiratory allergy in the Mediterranean area[5-6]. Ole e 1 is the major marker for primary olive pollen allergy and sensitization prevalence is about 70% within olive allergy patients[7]. Ole e 7 (LTP) allergy prevalence is 50% and Ole e 9 at 68%[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, as the flowering season coincides with that of birch. Ash may locally be as important as birch in the elicitation of spring pollinosis[1,8]. Although Fra e 1 is the major allergen for ash pollen-sensitization, cross-reactivity between Fra e 1and Ole e 1 in olive is so pronounced that Ole e 1 serves as a very good marker allergen for the diagnosis of ash pollen allergy[7].

London plane tree – *Platanus acerifolia* – (Pla a)

Plane trees are known as"street trees" and are found planted practically anywhere in the world. Recombinant Pla a 1 is a specific marker allergen suitable for discriminating between genuine plane tree pollen sensitization and cross-reactivity[7, 9]. Pla a 1 is a major plane tree pollen allergen recognized by up to 90% of plane tree-allergic patients[9-10]. Pla a 3 is an nsLTP which cross-reacts with other LTPs in e.g. fruits[11-12] sharing a 50% squence identity with Pru p 3[12]. Pla a 3 is not available on ImmunoCAP. However, Pla a 3, as well as the plane-tree specific and major allergen Pla a 1 and Pla a 2 are available on ImmunoCAP ISAC.

Cypress – *Cupressus arizonica* – (Cup a)

Cypresses are common ornamental trees found extensively in Southern Europe[13] but also can be found globally including North America and Japan[14]. Cedars are other members of the *Cupressaceae* family and IgE cross-react with similar species[15-16]. Cypress trees bloom in the winter and may cause winter respiratory allergy[7]. Winter pollen allergies are often misdiagnosed since symptoms are occurring during winter and are very similar to perennial allergies like dust mite allergy[7,17]. Rhinitis is the most prevalent symptom of cypress pollen, while conjunctivitis can be quite severe[15]. Component testing may help to better management of the patients[18-19].

Four allergens from *Cupressus arizonica* have been described, including the major allergen. Cup a 1[13,20-21]; Cup a 2 (polygalacturonase); Cup a 3 (thaumatin); and Cup a 4 (polcalcin). Cup a 1 is a specific marker for primary sensitization to *Cupressaceae* pollen[16]. 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), there is extensive cross-reactivity between these closely related species[7].

Available ImmunoCAP Allergen Products*

Italian cypress – Whole allergen – t23
Cypress – Whole allergen – t222
Olive – Whole allergen – t9
London plane – Whole allergen – t11

Component		Code
nCup a 1*	Pectate lyase-CCD bearing protein	t226
rOle e 1	Common olive group 1	t224
rOle e 7	LTP	t227
rOle e9	Glucanase	t240
rPla a 1	Invertase inhibitor	t241
CCD	MUXF3 from Bromelain	o214

*Complete product names on page 79.

Clinical Relevance

Identifying primary allergy to different trees and utilisation in AIT management[22-24].

Interpreting the results

Tree Pollen	Component	Protein	Code	Interpretation
Cypress, t23	nCup a 1*	Pectate lyase	t226	Primary sensitizer/major allergen in Cupressace trees. Good candidate for AIT[7,13,16,18, 21-25]
Olive/Ash t9 / t25	rOle e 1	Common Olive group 1	t224	Primary sensitizer/major allergen Also marker for ash tree sensitization. Good candidate for AIT[5-7,21-25]
Olive, t9	rOle e 7	LTP	t227	Minor allergen[5-7,25]
Olive, t9	rOle e 9	1 3-beta glucanase	t240	Major allergen[5-7,25]
London Plane Tree, t11	rPla a 1	Putative Invertase inhibitor	t241	Primary sensitizer/major allergen indicating Plane tree pollen sensitization. Good candidate for AIT[7,9-10,21-25]

**nCup 1 is purified from a native allergen source and contains CCD*

For other sources of common plant allergen cross-reactions also consider CCD, profilins and polcalcins.

References

1. García BE et al. Oleaceae-induced pollinosis in an area with exposure to olive and ash trees. Journal of Investigational Allergology and Clinical Immunology 2011;21(1):34–37.
2. Castro AJ et al. Pla l 1 and Ole e 1 pollen allergens share common epitopes and similar ultrastructural localization. J Investig Allergol Clin Immunol 2007;17 Supplement 1:41–47.
3. Rodríguez R et al. Olive pollen recombinant allergens: value in diagnosis and immunotherapy. J Investig Allergol Clin Immunol 2007;17 Suppl 1:4–10.
4. Rossi RE et al. Sensitization profiles in polysensitized patients from a restricted geographical area: Further lessons from multiplexed component resolved diagnosis. European Annals of Allergy and Clinical Immunology 2011;43(6):171–175.
5. Barber D et al. Understanding patient sensitization profiles in complex pollen areas: A molecular epidemiological study Allergy 2008;63(11):1550–1558.
6. Quiralte J et al. Modelling diseases: The allergens of Olea europaea pollen. J Investig Allergol Clin Immunol 2007;17 Suppl 1:24–30.
7. 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.
8. Hauser M et al. Pan allergens and their impact on the allergic patient. Allergy, Asthma & Clinical Immunology 2010; 6(1):1–14.
9. Asturias JA et al. Purification and characterization of Pla a 1, a major allergen from Platanus acerifolia pollen. Allergy 2002;57(3):221–7.
10. Asturias J et al. The major Platanus acerifolia pollen allergen Pla a 1 has sequence homology to invertase inhibitors. Clin Exp Allergy 2003;33(7):978-985.
11. Lauer I et al. Identification of a plane pollen lipid transfer protein (Pla a 3) and its immunological relation to the peach lipid-transfer protein, Pru p 3. Clin Exp Allergy 2007;37:261-269.
12. Scala E et al. Lipid transfer protein sensitization: reactivity profiles and clinical risk assessment in an Italian cohort. Allergy 2015;70:933-943.
13. Arilla MC et al. Quantification of the Major Allergen from Cypress (Cupressus arizonica) Pollen, Cup a 1, by Monoclonal Antibody-Based ELISA. Int Arch Allergy Immunol. 2004 May;134(1):10-6. Epub 2004 Mar 25
14. Di Felice G et al. Cupressaceae Pollinosis: Identification, Purification and Cloning of Relevant Allergens. Int Arch Allergy Immunol 2001;125:280-289.
15. Charpin D et al. Cypress Pollinosis: from Tree to Clinic. Clin Rev Allergy Immunol. 2017 Apr 11 doi: 10.1007/s12016-017-8602-y. [Epub ahead of print].
16. Domínguez-Ortega J et al. Prevalence of allergic sensitization to conifer pollen in a high cypress exposure area. Allergy Rhinol (Providence). 2016 Jan 1;7(4):200-206.
17. Caimmi D et al. Epidemiology of cypress pollen allergy in Montpellier. J Investig Allergol Clin Immunol. 2012;22(4):280-5.
18. Aceituno E et al. Molecular cloning of major allergen from Cupressus arizonica pollen: Cup a 1.Clin Exp Allergy 2000;30:1750–1758.

19. WHO/IUIS Allergen Nomenclature Sub-committee. http://www.allergen.org.
20. Douladiris N et al. A molecular diagnostic algorithm to guide pollen immunotherapy in Southern Europe: towards component resolved management of allergic diseases. Int Arch Allergy Immunol 2013;162:163-172.
21. Asam C et al. Tree pollen allergens - an update from a molecular perspective. Allergy 2015:70:1201-1211.
22. Schmid-Grendelmeier P. Recombinant allergens. For routine use or still only science? Hautarzt. 2010; 61(11): 946–53.
23. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
24. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
25. 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.

Pollen – Weeds

Common Ragweed – *Ambrosia artemisifolia* (Amb a)
Mugwort – *Artemisia vulgaris* (Art v)
Wall Pellitory – *Parietaria judaica*
(Par j) English Plantain – *Plantago lanceolata* (Pla l)
Saltwort – *Salsola kali* (Sal k)

Weed allergy diagnosis can be unclear and difficult to diagnose due to frequent poly-sensitizations and inconclusive anamnesis due to overlapping flowering seasons with other pollens such as birch and grass[1-2]. Cross-reactions are expected between different weed species when botanically closely related. Apart from profilin and CCDs, mugwort and ragweed pollen contain a number of other cross-reactive allergens. Cross-reactive IgE antibodies can lead to clinically significant allergic reactions[3-4]. Furthermore, mugwort, ragweed, and Timothy grass pollen share IgE epitopes with glycoprotein containing latex allergens, this presence of common epitopes might in part explain clinical symptoms in patients allergic to pollen on contact with latex[5].

Pollen-food syndromes driven by weed pollen are mainly generated by mugwort and ragweed pollen. As well as Oral Allergy Syndrome (OAS) more severe allergy is reported such as celery-mugwort-spice syndrome[6-9].

Available ImmunoCAP Allergen Products*

Common Ragweed – Whole allergen – w1
Mugwort – Whole allergen – w6
Wall Pellitory – Whole allergen – w21
Plantain (English) – Whole allergen – w9
Saltwort – Whole allergen – w11

Component		Code
nAmb a 1	Pectate lyase	w230
nArt v 1	Defensin-like protein	w231
nArt v 3	LTP	w233
rPar j 2	LTP	w211
rPla l 1	Ole e 1 like protein	w234
nSal k 1*	Pectin methylesterase	w232

Clinical Relevance*

Identifying primary allergy to different trees and utilisation in AIT management[1-2,10-13]

*Complete product names on page 79.

Interpreting the results

Weed Pollen	Component	Protein	Code	Interpretation
Ragweed, w1	nAmb a 1	Pectate lyase	w230	Primary sensitizer/major allergen Good candidate for AIT[1-2,10-13]
Mugwort, w6	nArt v 1	Defensin-like protein	w231	Primary sensitizer/major allergen Good candidate for AIT[1-2,10-13]
	nArt v 3	LTP	w233	Major allergen[1-2,13]
Parietaria/ Wall pellitory, w21	rPar j 2	LTP	w211	Primary sensitizer/major allergen Good candidate for AIT[1-2,10-13]
Plantain, w9	rPla l 1	Ole e 1 like protein	w234	Primary sensitizer/major allergen Good candidate for AIT[1-2,10-13]
Saltwort, w11	nSal k 1*	Pectin methylesterase	w232	Primary sensitizer/major allergen Good candidate for AIT[1-2,10-13]

**nSal k 1 is purified from a native allergen source and contains CCD, nAmb a 1 is also a purified native component but does not contain CCD.*

For other sources of common plant allergen cross-reactions also consider CCD, profilins and polcalcins.

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.
2. Gadermaier G et al. Allergens of weed pollen: An overview on recombinant and natural molecules. Methods 2014;66;55-66.
3. Hirschwehr R et.al, Identification of common allergenic structures in mugwort and ragweed pollen. J Allergy Clin Immunol 1998;101(2 Pt 1):196 206.
4. Asero R et al. Concomitant sensitization to ragweed and mugwort pollen: who is who in clinical allergy? Ann Allergy Asthma Immunol 2014;113:307-313.
5. Fuchs T et.al Natural latex, grass pollen, and weed pollen share IgE epitopes. J Allergy Clin Immunol 1997;100(3):356-64.
6. Helbling A. Food allergy. [German] Ther Umsch 1994;51(1):31-7.
7. Egger M et al. Pollen food syndromes associated with weed pollinosis: an update from the molecular point of view. Allergy 2006;61:461-476.
8. van Toorenenbergen AW et al. Demonstration of spice-specific IgE in patients with suspected food allergies. J Allergy Clin Immunol 1987;79(1):108-13.
9. Jensen-Jarolim E et al. Characterization of allergens in Apiaceae spices: anise, fennel, coriander and cumin. Clin Exp Allergy 1997;27(11):1299-306.

10. Schmid-Grendelmeier P. Recombinant allergens. For routine use or still only science? Hautarzt. 2010; 61(11): 946–53.
11. Canonica GW, et al. AWAO -ARIA- GA2LEN concenus document on molecular-based allergy diagnostics World Allergy Organization Journal 2013;6(1):17. 7.
12. Asero R. Component-resolved diagnosis-assisted prescription of allergen-specific immunotherapy: a practical guide Eur Ann Allergy Clin Immunol. 2012;44(5):183-7.
13. 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.

Molds

There is current evidence to demonstrate a close association between fungal sensitization and asthma severity. Many airborne fungi are involved, including species of *Alternaria*, *Aspergillus*, *Cladosporium* and *Penicillium*, and exposure may be indoors, outdoors or both. Fungal sensitization is common in asthmatic patients in urban settings and is associated with broader sensitization to non-fungal allergens and to increased risk of life-threatening asthma[1-2]. The term “severe asthma with fungal sensitization” (SAFS) has been proposed. However, it is recognised that enhanced and precise definition of fungal sensitization will require improvements in diagnostic testing[2-4]. This can be facilitated by component testing[5-7].

References

1. Medrek SK et al. Fungal sensitization is associated with increased risk of life-threatening asthma. J Allergy Clin Immunol Pract. 2007;5:1025-31.
2. Denning DW et al. The link between fungi and severe asthma: a summary of the evidence. Eur Respir J. 2006 Mar;27(3):615-26.
3. Rick EM et al. Allergic Fungal Airway Disease. J Investig Allergol Clin Immunol. 2016;26(6):344-354.
4. Castanhinha S et al. Pediatric severe asthma with fungal sensitization is mediated by steroid-resistant IL-33.J Allergy Clin Immunol. 2015 Aug;136(2):312-22.
5. Moreno A et al. Orthologous Allergens and Diagnostic Utility of Major Allergen Alt a 1. Allergy Asthma Immunol Res. 2016 Sep;8(5):428-37.
6. Gabriel MF et al. Alternaria alternata allergens: Markers of exposure, phylogeny and risk of fungi-induced respiratory allergy. Environ Int. 2016 Apr-May;89-90:71-80.
7. Canonica GW et al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 2013 3;6(1):17.

Alternaria alternata – (Alt a)

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[1-5]. Asthma in children with *Alternaria* sensitization has been reported to persist beyond age 11 years, compared to asthma in individuals who were negative[6]. *Alternaria*-sensitized patients may also be at risk for allergic rhinitis[7], and the most severe cases of rhinitis may be attributable to *Alternaria* sensitivity[8-9].

Alt a 1 is the major *Alternaria* allergen causing sensitization in asthmatics and has been reported as the main elicitor of airborne allergies in patients affected by a mold allergy. Alt a 1 is considered a marker of primary sensitization to *A. alternata*[3,5-7,10]. A vast majority (80-100%) of *Alternaria* sensitized patients have specific IgE to Alt a 1[11-13]. Alt a 1 is a highly allergenic molecule allowing sensitive and specific diagnosis of *Alternaria* allergy[11,14-16].

Available ImmunoCAP Allergen Products*

Alternaria alternata – Whole allergen – m6

Component		Code
rAlt a 1	unknown	m229

*Complete product names on page 79.

Clinical Relevance

Identifying primary sensitization to *Alternaria*.

Interpreting the results

m6	Alt a 1	Interpretation
+/-	+	Major allergen. Primary sensitization to *Alternaria*. Risk marker for severe asthma[1-17]

References

1. Bush RK and Prochnau JJ. Alternaria-induced asthma. J Allergy Clin Immunol 2004; 113:227–34.
2. Black PN et.al. Sensitivity to fungal allergens is a risk factor for life-threatening asthma. Allergy. 2000 May;55(5):501-4.
3. Vailes LD et al. IgE and IgG antibody responses to recombinant Alt a 1 as a marker of sensitization to Alternaria in asthma and atopic dermatitis. Clin Exp Allergy. 2001 Dec;31(12):1891-5.
4. Downs SH et al. Clinical importance of alternaria exposure in children. Am J Respir Crit Care Med 2001;164:455–9.
5. Halonen M et al. Alternaria as a major allergen for asthma in children raised in a desert environment. Am J Respir Crit Care Med 1997;155:1356–61.
6. Halonen M et al. Two subphenotypes of childhood asthma that differ in maternal and paternal influences on asthma risk. Am J Respir Crit Care Med 1999;160(2):564-70.
7. Corsico R et al. Prevalence of sensitization to Alternaria in allergic patients in Italy Ann Allergy Asthma Immunol 1998;80(1):71-6.
8. Dowaisan A et al. Sensitization to aeroallergens among patients with allergic rhinitis in a desert environment. Ann Allergy Asthma Immunol 2000;84(4):433-8.
9. Bartra J et al. Sensitization to Alternaria in patients with respiratory allergy. Front Biosci (Landmark Ed). 2009 Jan 1;14:3372-9.
10. Kustrzeba-Wójcicka I et al Alternaria alternata and its allergens: a comprehensive review. Clin Rev Allergy Immunol. 2014 Dec;47(3):354-65.
11. Twaroch TE et al. Carrier-Bound Alt a 1 Peptides without Allergenic Activity for Vaccination Against Alternaria Alternata Allergy. Clin Exp Allergy 2012; 42(6):966-975.
12. Unger A et al. Clinical testing of recombinant allergens of the mold Alternaria alternata. Int Arch Allergy Immunol 1999;118:220–1.
13. De Vouge MW et al. Isolation and expression of a cDNA clone encoding an Alternaria alter- nata Alt a 1 subunit. Int Arch Allergy Immunol 1996;111:385–95.
14. Postigo I et al. Diagnostic value of Alt a 1, fungal enolase and manganese-dependent superoxide dismutase in the component-resolved diagnosis of allergy to Pleosporaceae. Clin Exp Allergy. 2011 Mar;41(3):443-51.
15. Moreno A et al. Orthologous Allergens and Diagnostic Utility of Major Allergen Alt a 1. Allergy Asthma Immunol Res. 2016 Sep;8(5):428-37.
16. Gabriel MF et.al. Alternaria alternata allergens: Markers of exposure, phylogeny and risk of fungi-induced respiratory allergy. Environ Int. 2016 Apr-May;89-90:71-80.
17. 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.

Aspergillus fumigatus – (Asp f)

Aspergillus fumigatus causes the most common form of Allergic Bronchopulmonary Mycosis (ABPM), and is referred to as Allergic Bronchopulmonary Aspergillosis (ABPA). IgE sensitization tests are used as part of routine workup for diagnosing ABPA[1]. Genuine *A. fumigatus* sensitization is not always easily identifiable[1]. Other fungi species share cross reactive pan allergens with *A. fumigatus* which can cause non-specific test results. Therefore the use of specific IgE components for *A. fumigatus* can aid the identification of primary *A. fumigatus* sensitization[2].

Recent studies investigating ABPA demonstrated that ImmunoCAP Allergen Components could differentiate ABPA individuals from those with asthma and sensitized to *Aspergillus*[3-6]. Asp f 1 is major allergen, species specific and shares no homology with any known fungal genome[4]. Additionally it is not produced in spores but in germination and growth[4-6]. Asp f 2 is further species specific allergen and present in 96% frequency of sensitization with ABPA[1]. Asp f 4 has also been identified as a specific allergen in studies that used ImmunoCAP Allergen components[1-2,4,7-8]. Asp f 3 and Asp f 6 are described as cross-reactive allergens[3-6].

Available ImmunoCAP Allergen Products*

Aspergillus fumigatus – Whole allergen – m3

Component		Code
rAsp f 1	Ribotoxin	m218
rAsp f 2	Unknown	m219
rAsp f 3	Peroxisomal protein	m220
rAsp f 4	Unknown	m221
rAsp f 6	MnSOD	m222

*Complete product names on page 79.

Clinical Relevance

Helping understanding primary *Aspergillus fumigatus* sensitization, differentiating ABPA from asthma and sensitized patients.

Interpreting the results

m3	Asp f 1	Asp f 2	Asp f 3	Asp f 4	Asp f 6	Interpretation
+/-	+					Primary sensitization to *Aspergillus fumigatus*[1-2,4,7-8]
+/-		+				Primary sensitization to *Aspergillus fumigatus*[1-2,4,7-8]
+/-				+		Primary sensitization to *Aspergillus fumigatus*[1-2,4,7-8]
+/-			+			Likely cross sensitization from other mould species. Primary allergen should be identified[3-8]
+/-					+	Likely cross sensitization from other mould species. Primary allergen should be identified[3-8]

References

1. Fukutomi Y et al. Serological diagnosis of allergic bronchopulmonary mycosis: Progress and challenges. Allergology International 2016;65:30-36.
2. Carsin A et al. Aspergillus fumigatus in cystic fibrosis: An update on immune interactions and molecular diagnostics in allergic bronchopulmonary aspergillosis. Allergy. 2017;72:1632–1642.
3. Bowyer P et al. Relative reactivity of Aspergillus allergens used in serological tests Medical Mycology 2006;44:S23-S28.
4. H. Tanimoto et al. Molecular-based allergy diagnosis of allergic bronchopulmonary aspergillosis in Aspergillus fumigatus-sensitized Japanese patients Clinical & Experimental Allergy 2015;45, 1790–1800 + erratum Clin Exp Allergy 2016;46(2):381.
5. Kurup VP. Aspergillus antigens: which are important? Medical Mycology Supplement 1 2005;43 (1): s189 - S196.
6. Canonica GW, et al. A WAO -ARIA- GA2LEN consensus document on molecular-based allergy diagnostics World Allergy Organ J 2013;6(1):17. 7.
7. 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.
8. 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.

Venoms

Up to 50% of patients with suspected honey bee or common wasp allergy test postive when using extract testing[1]. True double allergic reactivity to both bee and wasp is not clinically common[1-3]. In many cases double venom IgE positivity can be caused by cross-reactions to CCDs[1-2]. Recombinant venom components do not carry CCD and therefore provide greater diagnostic specificity, useful when making decision such as to start AIT[4-6]. Low level specific IgE below 0.35 kU_A/l can be relevant when using components and indicative of venom allergy[6-7], so measuring down to 0.1 kU_A/l can be important.

Common Wasp – *Vespula vulgaris*
Paper wasp – *Polistes dominulus*

Ves v 1 and Ves v 5 are major allergens from common wasp and have demonstrated clinical sensitization rates, of between 33.3 - 54% and 84.5 - 100% respectively[7]. The combination of the two tests in a study by Korosec et al provided sensitivity of 92%[9]. Paper wasp is common in Southern Europe and other parts of the world and Pol d 5 is a marker for sensitization to paper wasp[1-2,7].

Honey Bee – *Apis mellifera*

The picture for bee sensitivity seems more complex than for wasp and can involve more varied sensitization patterns to major components[7]. Api m 1, Api m 2, Api m 3, Api m 5 and Api m 10 are all major allergens within bee venom allergy[7]. Api m 1 and Api m 10 demonstrate the highest clinical sensitization rates, ranging from 57 - 97% for Api m 1 and 51.5 - 61.8 for Api m 10[7]. It has recently been shown that using an increasing number of bee components can improve bee sensitivity[8]. Api m 3 and Api m 10 can be absent or/underrepresented in VIT extracts[10-11], thus venom AIT in patients sensitized to these components may be less efficient.

Patients with suspected venom allergy should also be tested for tryptase[2-3,7]. Patients with high basal levels of tryptase should be investigated for mastocytosis since these patients have higher risk for severe reactions during venom immunotherapy[2-3,7,12]. It is recommended that special attention should be paid to patients who have high baseline tryptase measurements[2-3,7,12].

Available ImmunoCAP allergen products*

Honey bee – Whole allergen – i1
Common wasp (Yellow jacket) – Whole allergen – i3
Paper wasp – Whole allergen – i4

Component		Code
rApi m 1	Phospholipase A2	i208
rApi m 2	Hyaluronidase	i214
rApi m 3	Acid phosphatase	i215
rApi m 5	Dipeptidyl peptidase	i216
rApi m 10	Icarapin	i217
rVes v 1	Phospholipase A1	i211
rVes v 5	Antigen 5	i209
rPol d 5	Antigen 5	i210
CCD	MUXF3 from Bromelain	o214

*Complete product names on page 79.

Clinical Relevance

Helping differentiating primary bee and wasp sensitization from cross-reactivity. An aid to select proper treatment extract in venom AIT[4-9,13].

Interpreting the results

i1, i3, i4	Api m 1	Api m 2	Api m 3	Api m 5	Api m 10	Ves v 1	Ves v 5	Pol d 5	CCD	Interpretation
+/-	+									Primary sensitization to Honey bee, Good candidate for AIT. Clinical sensitivity of Honey bee Components combined >90%[4-8,13]
+/-		+								
+/-			+							
+/-				+						
+/-					+					
+/-						+				Primary sensitization to Common wasp, a good candidate for Common wasp AIT. Clinical sensitivity of wasp components combined >90%[4-7,9,13]
+/-							+			
+/-								+		Primary sensitization to paper wasp[4-7,9,13]
+/-									+	If venom components are negative and CCD positive. Further investigations may be necessary to identify underlying source[1-2,7,13]

References

1. Spillner E et al. Hymenoptera allergens: from venom to "venome". Frontiers in immunology 2014; 5:1-7.
2. Biló B et al. EAACI Interest Group on Insect Venom Hypersensitivity. Diagnosis of Hymenoptera venom allergy. Allergy 2005;60:1339-1349.
3. Bonifazi F et al. and EAACI Interest Group on Insect Venom Hypersensitivity. Prevention and treatment of hymenoptera venom allergy: guidelines for clinical practice. Allergy 2005;60:1459-1470.
4. Muller U et al. IgE to recombinant allergens Api m 1, Ves v 1, and Ves v 5 distinguish double sensitization from cross-reaction in venom allergy. Allergy 2012;67:1069–1073.
5. Mittermann I et al. Recombinant allergen-based IgE testing to distinguish bee and wasp allergy et al. June 2010. Volume 125, Issue 6, 1300–1307.e3.
6. Michael J et al. Added sensitivity of component-resolved diagnosis in hymenoptera venom-allergic patients with elevated serum tryptase and/or mastocytosis. Allergy 2016;71:651–660.
7. 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.
8. Kohler et al. Component resolution reveals additional major allergens in patient's with honeybee venom allergy. J Allergy Clin Immunol 2014;133:1383-9.
9. Korošec P et al. High sensitivity of CAP-FEIA rVes v 5 and rVes v 1 for diagnosis of Vespula venom allergy J Allergy Clin Immunol. 2012 May;129(5):1406-8.
10. Grunwald T et al., Molecular cloning and expression in insect cells of honeybee venom allergen acid phosphatase (Api m 3). Allergy Clin Immunol 2006;117:848-54.
11. Blank S et al. Api m 10, a genuine A. mellifera venom allergen, is clinically relevant but underrepresented in therapeutic extracts. Allergy 2011;66:1322-1329.
12. Bonadonna P et al. Clonal mast cell disorders in patients with systemic reactions to Hymenoptera stings and increased serum tryptase levels. J Allergy Clin Immunol 2009;123:680-6.
13. 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.

Occupational Allergens

Latex – *Hevea brasiliensis* (Hev b)

Latex allergy is often associated with an occupational exposure and can trigger contact urticaria but also severe and even life-threatening allergic reactions. IgE to Hev b 5 and Hev b 6 is often linked with occupational aero exposure to latex e.g. in healthcare workers and food handling personnel using latex gloves[1-5]. Hev b 1 and Hev b 3 are insoluble molecules and therefore allergen transmission comes via direct contact e.g. in patients with histories of multiple operations such as spina bifida patients[5-6]. Latex components are useful tools in resolving specific latex sensitization from cross reactivity due to e.g. profilin (Hev b 8) and CCDs[7-9].

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. Hev b 11 is a class 1 chitinase which can be involved in latex food cross-reactions[10,11]. Patients with latex-pollen syndrome are often sensitised to MUXF3 (CCD) and/or Hev b 8 (profilin)[5,12].

Available ImmunoCAP allergen products*

Latex – Whole allergen – k82

Component		Code
rHev b 1	Rubber elongation factor	k215
rHev b 3	Small rubber particle protein	k217
rHev b 5	Acidic structural protein	k218
rHev b 6.02	Prohevein	k220
rHev b 8	Profilin	k221
rHev b 11	Class 1 chitinase	k224
CCD	MUXF3 from Bromelain	o214

Clinical relevance

Understanding risk and cross-reactions.

*Complete product names on page 79.

Interpreting the results

k82	Hev b 1	Hev b 3	Hev b 5	Hev b 6	Hev b 8	Hev b 11	CCD	Interpretation
+/-	+							Primary sensitization to latex[5-6,13]
+/-		+						Primary sensitization latex[5-6,13]
+/-			+					Primary sensitization to latex[5-6,13]
+/-				+		+		Primary sensitization to latex, also associated with latex fruit syndrome. Hev b 6, prohevein and Hev b 11 class 1 chitinase can cross-react with other foods and plants such as avocado, kiwi, chestnut or banana[1-5,13]
+/-					+			Low risk for latex allergy. Likely cross sensitization. Primary allergen should be identified[5,7-9,12-13]
+/-							+	Low risk for latex allergy. Likely cross sensitization. Primary allergen should be identified[5,7-9,12-13]

References

1. Sutherland MF et al. Specific monoclonal antibodies and human immunoglobulin E show that Hev b 5 is an abundant allergen in high protein powdered latex gloves. Clin Exp Allergy 2002;32(4):583-589.
2. Rozynek P et al. Cloning, expression and characterization of the major latex allergen prohevein. Clin Exp Allergy 1998;28(11):1418-1426.
3. Raulf-Heimsoth M et al. Characterization of B- and T-cell responses and HLA-DR4 binding motifs of the latex allergen Hev b 6.01 (prohevein) and its post-transcriptionally formed proteins Hev b 6.02 and Hev b 6.03. Allergy 2004;59(7):724-733.
4. Vandenplas O et al. The role of allergen components for the diagnosis of latex-induced occupational asthma. Allergy 2016;71:840–849.
5. 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.
6. Wagner B, et al. Hev b 7 is a Hevea brasiliensis protein associated with latex allergy in children with spina bifida. J Allergy Clin Immunol 2001;108(4):621-627.

7. Ebo DG et al. Component-resolved diagnosis from latex allergy by micro-array. Clin Exp Allergy 2010;40(2):348-358.

8. Ott H et al. Microarrays of recombinant Hevea brasiliensis proteins: A novel tool for the component- resolved diagnosis of natural rubber latex allergy. J Investig Allergol Clin Immunol 2010;20(2):129-138.

9. 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(1):11.

10. O'Riordain G et al. Cloning and molecular characterization of the Hevea brasiliensis allergen Hev b 11, a class I chitinase. Clin Exp Allergy 2002;32(3):455-62

11. Nettis E Diagnosis of latex allergy: the importance of hev B 11. Int Arch Allergy Immunol. 2012;159 (2) 147-8.

12. Garnier L et al. Molecular allergens in the diagnosis of latex allergy. Eur Ann Allergy Clin Immunol 2012;44(2):73–79.

13. 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.

Introduction to Allergen Micro Array

ImmunoCAP ISAC

Allergen micro-arrays have been around since the late 1990s and therefore in some ways are not new products. What is new is that in the last few years' arrays have improved in analytical performance, reporting software and of course there is also a better clinical understanding of how to interpret positive and negative results.

Recent studies and reviews have shown comparable performance of ImmunoCAP ISAC versus other existing techniques such as extract based skin prick tests and specific IgE blood tests[1]. Furthermore ImmunoCAP ISAC can provide further refined information or change diagnosis compared to standard assessment or testing. In a Swedish asthma study ImmunoCAP ISAC provided more refined IgE characterisation in 47% of patients compared to standard extract-based methods[2]. Whereas in a recent atopic dermatitis study 70% of patients had a change in diagnosis when ImmunoCAP ISAC was included in the workup[3].

Besides applications in research, multiplex in-vitro diagnostics are increasingly being used to answer clinical questions in regular allergy clinics. The combination of microarray, single component allergens and extract based tests allows a much more comprehensive view of the sensitization status of the patient. Together with clinical history it is possible to quickly identify clinical phenotypes especially in multi-sensitized patients[4-8].

The currently available multiplex systems, are just the beginning of a development that will significantly affect clinical allergy in the coming years. New allergens and technological advancement will contribute to product changes. Allergen components have been and will be removed and added, based on factors such as new allergen discovery, availability and clinical experience of the current version of a product.

On ImmunoCAP ISAC there are more than 100 allergen components representing many different protein families, which gives a good "snapshot" of a sensitization profile. The profile together with symptoms and clinical history provides a detailed foundation for clinical assessment.

ImmunoCAP ISAC can sometimes generate a lot of IgE results and careful clinical interpretation and knowledge of allergen proteins is essential to interpret a patient report. Much of the content of Go Molecular Books 1 and 2 is relevant to interpreting allergen array. A software tool is available for ImmunoCAP ISAC laboratories, which provides additional interpretational support.

Facts on ImmunoCAP ISAC 112$_{E112i}$

ImmunoCAP ISAC:

- Is a multiplex allergen micro-array
- ImmunoCAP ISAC contains 112 allergen components from 49 allergen sources representing different protein families - see separate list of allergens
- Enables simultaneous measurement of IgE to the 112 allergen components in a single step
- Small sample volume needed: just 30µl serum sample or plasma
- Capillary or venous blood can be used
- ImmunoCAP ISAC measures IgE in ISU-E which stands for - ISAC Standard Units ImmunoIglobulin E
- The results are presented semi-quantitatively in 4 classes each corresponding to a concentration range
- Is a complementary technology that should be used in conjunction with clinical history and other sensitization tests

Advantages of ImmunoCAP ISAC

Advantages can obviously be looked at in different perspectives, in the research arena ImmunoCAP ISAC could seem an easy choice of a diagnostic test - you get a lot of allergen specific IgE test results from just a small amount of precious serum (30µl). These advantages apply to the clinical environment

Technical feature	Clinical Advantages
Wide number of allergen components from many different protein families	• Better coverage of allergen sources overall • Wider coverage to identify primary sensitizer(s) • Can make economic sence when tests with a lot of allergens are needed
Multiplexed protein families	• Allow extrapolations of probable sensitization to other allergens sources not actually included, by using surrogate allergen components on the array • Help understand cross-reactions between different species • Help understand different syndromes e.g. pollen-food
Recombinant or purified allergen components	• Recombinant/purified native allergen components are pure consisting of only one type of protein making them highly specific for measuring antibodies of one type
Micro-array platform	• Small sample volume needed (30µl), giving more than 100 results
Good technical performance	• ImmunoCAP ISAC shows high sensitivity and specificity[9] and good correlation with other types of testing including specific IgE and skin prick[10-11]

too where blood volumes from children can be limited.

The above table gives an overview of some advantages of microarray.

Examples of the clinical relevance of ImmunoCAP ISAC include:

- Complex patient cases – patients with complex symptomology e.g. eczema and unstable asthma[5]
- Eczema patients – involving multiple allergens[3,12-15]
- Idiopathic anaphylaxis – ImmunoCAP ISAC identified further useful clinical information in 20% of this group of patients from a UK study[16]
- Multi-sensitized patients – e.g. patients with possible cross-reactions or genuine primary allergens. Many of the papers referenced in the section are citations which investigate multi-sensitized patients[12-19]
- Allergy work up for Immunotherapy patients[17-19]
- Food allergy investigations[20-22]
- Respiratory allergy[23-24]

References

1. Jensen-Jarolim E et al. Debates in allergy medicine: Molecular allergy diagnosis with ISAC will replace screenings by skin prick test in the future. World Allergy Organization Journal. 2017;10:33.
2. Onell A et al. Allergy testing in children with persistent asthma: comparison of four diagnostic methods. Allergy 2017;72: 590–597.
3. Foong R et al. Pilot study: assessing the clinical diagnosis of allergy in atopic children using a microarray assay in addition to skin prick testing and serum specific IgE. Clin Mol Allergy 2016; 14:8.
4. Canonica GW, et al. A WAO – ARIA – GA2LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J 2013;6(1):17.
5. 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.
6. 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.
7. Patelis A, et al. Multiplex component-based allergen microarray in recent clinical studies Clinical & Experimental Allergy. 2016;46:1022–1032.
8. Melioli G et al. Allergenius, an expert system for the interpretation of allergen microarray results. World Allergy Organ J 2014:7:15.
9. Panzner P et al. A comprehensive analysis of middle-European molecular sensitization profiles to pollen allergens. Int Arch Allergy Immunol. 2014;164:74–82.
10. Huss-Marp J et al. Comparison of molecular and extract-based allergy diagnostics with multiplex and singleplex analysis. Allergo J Int. 2015;24:46–53.
11. Williams P et al. Evaluation of a novel automated allergy microarray platform compared with three other allergy test methods. Clin Exp Immunol. 2016;184:1–10.
12. Fedenko E et al. Microarray-based IgE serology improves management of severe atopic dermatitis in two children. Pediatric Allergy and Immunology 2016;27;645–659.
13. Mari A et al. The IgE-microarray testing in atopic dermatitis: a suitable modern tool for the immunological and clinical phenotyping of the disease. Curr Opin Allergy Clin Immunol 11:438–444.
14. Ott H et al. Allergen microarrays: a novel tool for high-resolution IgE profiling in adults with atopic dermatitis Eur J Dermatol 2010; 20 (1): 54-61.
15. Choi JS et al. Clinical availability of component-resolved diagnosis using microarray technology in atopic dermatitis. Ann Dermatol. 2014;26:437–46.
16. Heaps A et al. The utility of the ISAC allergen array in the investigation of idiopathic anaphylaxis. Clin Exp Immunol. 2014 Aug;177(2):483-90.
17. Sastre J et al. How molecular diagnosis can change allergen-specific immunotherapy prescription in a complex pollen area. Allergy. 2012 May;67(5):709-11.
18. Asero R et al. Component-resolved diagnosis- assisted prescription of allergen specific immunotherapy: a practical guide. Eur Ann Allergy Clin Immunol 2012;44:183–7.
19. Melioli G et al. Potential of molecular based diagnostics and its impact on allergen immunotherapy. Asthma Research and Practice 2016 2:9.
20. Kukkonen A K et al. Ara h 2 and Ara 6 are the best predictors of severe peanut allergy: a double-blind placebo-controlled study. Allergy 2015;70:1239–1245.
21. D'Urbano L E et al. Performance of a component-based allergen-microarray in the diagnosis of cow's milk and hen's egg allergy. Clinical & Experimental Allergy. 2010;40;1561–1570.
22. Scala E et. al. Lipid transfer protein sensitization: reactivity profiles and clinical risk assessment in an Italian cohort. Allergy 2015;70:933–943.
23. Nordlund B et al. IgE antibodies to animal-derived lipocalin, kallikrein and secretoglobin are markers of bronchial inflammation in severe childhood asthma. Allergy 2012;67:661–9.
24. Konradsen JR et al. Allergy to Furry animals: New Insights, diagnostic approaches, and challenges. J Allergy Clin Immunol 2015;135:616-25.

Recommended further educational resources

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

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

Canonica GW, et al. A WAO – ARIA – GA2LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J 2013;6(1):17.

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.

Using ImmunoCAP Allergen Component tests

ImmunoCAP Allergen Components, singleplex as well as multiplex, are useful tools for the physician when investigating and explaining allergic reactions more in detail and to determine if cross-reacting IgE antibodies or primary sensitization causes them. However as with 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 on 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.

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.
2. 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.
3. Canonica GW et.al. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnostics. World Allergy Organ J. 2013 Oct 3;6(1):17.
4. Wickman M. When allergies complicate allergies. Allergy 2005;60(S79):14-18.
5. Van Hage M et.al. ImmunoCAP assays: Pros and cons in allergology. J Allergy Clin Immunol 2017;140:974-7.

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

**Not all ImmunoCAP Products are available in all regions/ countries*

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

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

Product description	Latin name	Code	Size	Art. no.	Barcode
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
Occupational / Enzymes					
Alkalase	*Alkalase*	k205	10	14-5126-01	C1F
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
nCar p 1 Papain, Papaya	*nCar p 1 Papain, Papaya*	k201	10	14-5130-01	BT0
nGal d 4 Lysozyme, Egg	*nGal d 4 Lysozyme, Egg*	k208	10	14-5128-01	C0T
Maxatase	*Maxatase*	k204	10	14-5129-01	C2F
Savinase	*Savinase*	k206	10	14-5132-01	C2R
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

**Not all ImmunoCAP Products are available in all regions/ countries*

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

Product description	Latin name	Code	Size	Art. no.	Barcode
Foods continued					
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
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
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 o 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 5	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*	

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

ImmunoCAP Allergen Components - Complete product names

ImmunoCAP Allergen f13, Peanut; ImmunoCAP Allergen f422, Allergen component rAra h 1 Peanut; ImmunoCAP Allergen f423, Allergen component rAra h 2 Peanut; ImmunoCAP Allergen f424, Allergen component rAra h 3 Peanut; ImmunoCAP Allergen f447, Allergen component rAra h 6 Peanut; ImmunoCAP Allergen f352, Allergen component rAra h 8 Peanut; ImmunoCAP Allergen f427, Allergen component rAra h 9 Peanut; ImmunoCAP Allergen f14, Soybean, ImmunoCAP Allergen f353, Allergen component rGly m 4 PR-10, Soy, ImmunoCAP Allergen f431, Allergen component nGly m 5 Beta-conglycinin, Soy, ImmunoCAP Allergen f432, Allergen component nGly m 6 Glycinin, Soy; ImmunoCAP Allergen f17, Hazel nut; ImmunoCAP Allergen f422, Allergen component rCor a 1 PR-10 Hazel nut; ImmunoCAP Allergen f425, Allergen component rCor a 8, Hazel nut; ImmunoCAP Allergen f440, Allergen component nCor a 9, Hazelnut; ImmunoCAP Allergen f439, Allergen component rCor a 14, Hazelnut; ImmunoCAP Allergen f256, Walnut; ImmunoCAP Allergen f441, Allergen component rJug r 1, Walnut; ImmunoCAP Allergen f442, Allergen component rJug r 3 LTP, Walnut; ImmunoCAP Allergen f202, Cashew nut; ImmunoCAP Allergen f443, Allergen component rAna o 3, Cashew nut; ImmunoCAP Allergen f18, Brazil nut; ImmunoCAP Allergen f354, Allergen component rBer e 1, Brazil nut; ImmunoCAP Allergen f449, Allergen Component rSes i 1, Sesame seed; ImmunoCAP Allergen f49, Apple; ImmunoCAP Allergen f237, Apricot; ImmunoCAP Allergen f95, Peach; ImmunoCAP Allergen f94, Pear; ImmunoCAP Allergen f255, Plum; ImmunoCAP Allergen f20, Almond; ImmunoCAP Allergen f343, Raspberry; ImmunoCAP Allergen f44, Strawberry; ImmunoCAP Allergen f419, Allergen component rPru p 1 PR-10, Peach; ImmunoCAP Allergen f420, Allergen component rPru p 3 LTP, Peach; ImmunoCAP Allergen f421, Allergen component rPru p 4 Profilin, Peach; ImmunoCAP Allergen f454, Allergen Component rPru p 7, Peach; ImmunoCAP Allergen f434, Allergen component rMal d 1 PR-10, Apple; ImmunoCAP Allergen f435, Allergen component rMal d 3 LTP, Apple; ImmunoCAP Allergen f4, Wheat; ImmunoCAP Allergen f98, Gliadin; ImmunoCAP Allergen f416, Allergen component rTri a 19 Omega-5 Gliadin, Wheat; ImmunoCAP Allergen f433, Allergen component rTri a 14 LTP, Wheat; ImmunoCAP Allergen f1, Egg white; ImmunoCAP Allergen f75, Egg yolk; ImmunoCAP Allergen f233, Allergen component nGal d 1 Ovomucoid, Egg; ImmunoCAP Allergen f232, Allergen component nGal d 2 Ovalbumin, Egg; ImmunoCAP Allergen f323, Allergen component nGal d 3 Conalbumin, Egg; ImmunoCAP Allergen k208, Allergen component nGal d 4 Lysozyme, Egg; ImmunoCAP Allergen f2, Milk; ImmunoCAP Allergen f76, Allergen component nBos d 4 Alpha-lactalbumin, Milk; ImmunoCAP Allergen f77, Allergen component nBos d 5 Beta-lactoglobulin, Milk; ImmunoCAP Allergen e204, Allergen component nBos d 6 BSA, Cow; ImmunoCAP Allergen f78, Allergen component nBos d 8 Casein, Milk; ImmunoCAP Allergen f27, Beef; ImmunoCAP Allergen f26, Pork; ImmunoCAP Allergen f88, Mutton; ImmunoCAP Allergen c74, Gelatin bovine; ImmunoCAP Allergen o215, Component nGal-alpha-1,3-Gal (alpha-Gal) Thyroglobulin, bovine; ImmunoCAP Allergen f24, Shrimp; ImmunoCAP Allergen f23, Crab; ImmunoCAP Allergen f37, Blue mussel; ImmunoCAP Allergen f351, Allergen component rPen a 1 Tropomyosin, Shrimp; ImmunoCAP Allergen d205, Allergen component rDer p 10 Tropomyosin, House dust mite; ImmunoCAP Allergen f3, Fish (cod); ImmunoCAP Allergen f42, Haddock; ImmunoCAP Allergen f41, Salmon; ImmunoCAP Allergen f206, Mackerel; ImmunoCAP Allergen f426, Allergen component rGad c1 Cod; ImmunoCAP Allergen f355, Allergen component rCyp c1 Carp; ImmunoCAP Allergen e1, Cat dander, ImmunoCAP Allergen e94, Allergen component rFel d 1 Cat, ImmunoCAP Allergen e220, Allergen component rFel d 2 Cat serum albumin, ImmunoCAP Allergen e228, Allergen component rFel d 4, Cat, ImmunoCAP Allergen e231, Allergen component rFel d 7, Cat; ImmunoCAP Allergen e5, Dog dander, ImmunoCAP Allergen e101, Allergen component rCan f 1 Dog, ImmunoCAP Allergen e102, Allergen component rCan f 2 Dog, ImmunoCAP Allergen e221, Allergen component nCan f 3 Dog serum albumin, ImmunoCAP Allergen e229, Allergen component rCan f 4, Dog, ImmunoCAP Allergen e226, Allergen component rCan f 5, Dog, ImmunoCAP Allergen e230, Allergen component rCan f 6, Dog; ImmunoCAP Allergen e3, Horse dander; ImmunoCAP Allergen e227, Allergen component rEqu c 1, Horse; ImmunoCAP Allergen d1, House dust mite; ImmunoCAP Allergen d2, House dust mite; ImmunoCAP Allergen d202, Allergen component nDer p 1, House dust mite; ImmunoCAP Allergen d203, Allergen component rDer p 2, House dust mite; ImmunoCAP Allergen d205, Allergen component rDer p 10 Tropomyosin, House dust mite; ImmunoCAP Allergen d209, Allergen component rDer p 23, House dust mite; ImmunoCAP Allergen g2, Bermuda grass; ImmunoCAP Allergen g6, Timothy; ImmunoCAP Allergen g216, Allergen component nCyn d 1 Bermuda grass; ImmunoCAP Allergen g205, Allergen component rPhl p 1 Timothy; ImmunoCAP Allergen g206, Allergen component rPhl p 2 Timothy; ImmunoCAP Allergen g208, Allergen component nPhl p 4 Timothy; ImmunoCAP Allergen g215, Allergen component rPhl p

ImmunoCAP Allergen Components - Complete product names

5b Timothy; ImmunoCAP Allergen g209, Allergen component rPhl p 6 Timoth; ImmunoCAP Allergen g210, Allergen component rPhl p 7 Timothy; ImmunoCAP Allergen g211, Allergen component rPhl p 11 Timoth; ImmunoCAP Allergen g212, Allergen component rPhl p 12 Profilin, Timothy; ImmunoCAP Allergen g213, Allergen component rPhl p 1, rPhl p 5b Timothy; ImmunoCAP Allergen g214, Allergen component rPhl p 7, rPhl p 12 Timothy; ImmunoCAP Allergen o214, Allergen component MUXF3 CCD, Bromelain; ImmunoCAP Allergen t3, Common silver birch; ImmunoCAP Allergen t215, Allergen component rBet v 1 PR-10, Birch; ImmunoCAP Allergen t216, Allergen component rBet v 2 Profilin, Birch; ImmunoCAP Allergen t220, Allergen component rBet v 4 Birch; ImmunoCAP Allergen t225, Allergen component rBet v 6 Birch; ImmunoCAP Allergen t221, Allergen component rBet v 2, rBet v 4 Birch; ImmunoCAP Allergen t23, Italian/Mediterranean/Funeral cypress; ImmunoCAP Allergen t222, Arizona cypress; ImmunoCAP Allergen t9, Olive; ImmunoCAP Allergen t11, Maple leaf sycamore, London plane; ImmunoCAP Allergen t226, Allergen component nCup a 1 Cypress; ImmunoCAP Allergen t224, Allergen Component rOle e 1, Olive; ImmunoCAP Allergen t227, Allergen component nOle e 7 LTP, Olive; ImmunoCAP Allergen t240, Allergen Component rOle e 9, Olive; ImmunoCAP Allergen t241, Allergen component rPla a 1, Maple leaf sycamore, London plane; ImmunoCAP Allergen w6, Mugwort; ImmunoCAP Allergen w21, Wall pellitory; ImmunoCAP Allergen w9, Plantain (English), Ribwort; ImmunoCAP Allergen w11, Saltwort (prickly), Russian thistle; ImmunoCAP Allergen w230, Allergen component nAmb a 1 Ragweed; ImmunoCAP Allergen w231, Allergen component nArt v 1 Mugwort; ImmunoCAP Allergen w233, Allergen component nArt v 3 LTP, Mugwort; ImmunoCAP Allergen w211, Allergen component rPar j 2 LTP, Wall pellitory; ImmunoCAP Allergen w234, Allergen component rPla l 1, Plantain; ImmunoCAP Allergen w232, Allergen component nSal k 1 Saltwort; ImmunoCAP Allergen m6, Alternaria alternate; ImmunoCAP Allergen m229, Allergen component rAlt a 1, Alternaria alternata; ImmunoCAP Allergen m3, Aspergillus fumigatus; ImmunoCAP Allergen m218, Allergen component rAsp f 1 Aspergillus fumigatus; ImmunoCAP Allergen m219, Allergen component rAsp f 2 Aspergillus fumigatus; ImmunoCAP Allergen m220, Allergen component rAsp f 3 Aspergillus fumigatus; ImmunoCAP Allergen m221, Allergen component rAsp f 4 Aspergillus fumigatus; ImmunoCAP Allergen m222, Allergen component rAsp f 6 Aspergillus fumigatus; ImmunoCAP Allergen i1, Honey bee venom; ImmunoCAP Allergen i3, Common wasp venom (Yellow jacket); ImmunoCAP Allergen i4, Paper wasp venom; ImmunoCAP Allergen i208, Allergen component rApi m 1 Phospholipase A2, Honey bee; ImmunoCAP Allergen i214, Allergen component rApi m 2, Honey bee; ImmunoCAP Allergen i215, Allergen component rApi m 3, Honey bee; ImmunoCAP Allergen i216, Allergen component rApi m 5, Honey bee; ImmunoCAP Allergen i217, Allergen component rApi m 10, Honey bee; ImmunoCAP Allergen i211, Allergen component rVes v 1 Phospholipase A1, Common wasp; ImmunoCAP Allergen i209, Allergen component rVes v 5 Common wasp; ImmunoCAP Allergen i210, Allergen component rPol d 5 European Paper wasp;; ImmunoCAP Allergen k82, Latex; ImmunoCAP Allergen k218, Allergen component rHev b 5 Latex; ImmunoCAP Rare Allergen k215, Allergen component rHev b 1 Latex; ImmunoCAP Rare Allergen k217, Allergen component rHev b 3 Latex; ImmunoCAP Rare Allergen k220, Allergen component rHev b 6.02 Latex; ImmunoCAP Rare Allergen k221, Allergen component rHev b 8 Profilin, Latex; ImmunoCAP Rare Allergen k224, Allergen component rHev b 11 Latex.

Notes

thermoscientific

thermofisher.com/phadia

Head office Sweden +46 18 16 50 00
Austria +43 1 270 20 20
Belgium (FR) +329 272 5780
(NL) +329 272 5780
Brazil +55 0800 0551 535
China +86 800 810 5118
Czech Republic +420 7250 84047
Denmark +45 70 23 33 06
Finland +358 10 3292 110
France +33 1 61 37 34 30
Germany +49 761 47 8050
Hong Kong +852 3107 7600
India +91 11 4937 5400
Ireland +44 1800 615 167
Italy +39 039 838 91
Japan +81 3 6872 6200
Korea +82 2 6196 5556~9
Norway +47 21 67 32 80
Portugal +351 21 423 5350
South Africa +27 11 792 6790
Spain +34 935 765 800
Sweden +46 18 16 60 60
Switzerland +41 43 343 40 50
Taiwan +886 2 8751 6655
The Netherlands +31 30 602 37 00
United Kingdom +44 1908 769110
USA +1 800 346 4364
Other countries +46 18 16 50 00

ThermoFisher SCIENTIFIC

75163.AL.GB1.EN.v1.19