

ImmunoCAP® ISAC IgE Allergy Profile

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Next to the prick test, the determination of allergen-specific IgE antibodies in serum has a key role in the detection of type I allergies. Typically, the CAP test (Thermo Fisher Scientific), which quantifies allergen-specific IgE antibodies in serum and permits the results' allocation to CAP classes from 1 to 6, is performed in this context. While the IgE detection using CAP test allows for the simultaneous determination of only a limited number of allergens, the ImmunoCAP® ISAC (Thermo Fisher Scientific) enables the concurrent analysis of 112 allergen components from 51 different allergen sources. Thus, this test facilitates the determination of a comprehensive specific IgE antibody profile. However, the essential difference with regard to the CAP test is that the ISAC assesses only IgE antibodies against relevant allergen components. In contrast to skin tests and classic specific IgE determination, native allergen extracts are not utilised. Therefore, results from the ISAC test differentiate between genuine primary sensitisations and cross-reactions. This additional information allows a better risk assessment regarding clinical manifestations. Contrary to common believe, allergen component diagnostics (molecular allergen diagnostics) is not more sensitive than the common CAP test. Therefore, this test has not to be considered as a classic screening test, but is a powerful tool for differential diagnostics for patients with polysensitisations.

Significant clinical indications for the ImmunoCAP® ISAC IgE allergy profile are:

1. Distinction between "only cross-reactivity" and genuine species-specific sensitisation
2. Identification of potential risks for reactions and type of reaction regarding certain allergic sensitisations
3. Assistance in the therapy and dietary selection, especially for patients with polysensitisations and positive IgE or prick test results regarding pollen-associated foods.

For targeted inquiries (e.g. clarification of relevance of peanut allergies, differentiation of bee and wasp venom allergies), the IgE CAP test can still be applied. For these inquiries, allergen component tests are available and German statutory health insurance companies do cover the costs.

Due to the large allergen spectrum and the small required sample size, this analysis is especially suitable for allergy diagnostics in children.

Method

ImmunoCAP® ISAC is a biochip-based semi-quantitative immunoassay (Fig. 1). Allergen components are immobilized on the biochip and react with specific IgE from the patient's sample. Bound IgE antibodies are determined with the help

of fluorescence technique. Test results are issued in ISAC Standardized Units (ISU) and indicate the specific IgE level. For allergens included in the test, please consult the enclosed list.

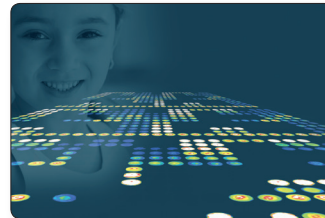


Fig. 1 With the help of fluorescent spots on the biochip, the reaction of allergens and IgE antibodies is evaluated. The intensity of the signals is proportional to the number of IgE antibodies bound to the allergen.

The principles of Molecular Allergy Diagnostics

Contrary to the prick test or conventional allergy IgE diagnostics, which are based on allergen extracts, molecular allergen diagnostics focus on sensitizations against single allergen components (Fig. 2). Those allergen components are either obtained from allergen extracts (native allergen components, labelled with "n", like in nMUXF3) or are produced in the recombinant manner (labelled with "r", like in rApi m 1). These components can be allocated to different protein groups and allow the discrimination of the detected sensitizations as well as the reaction's specificity. Table 1 on page 2 provides an overview of protein groups that are most frequently involved in allergies.

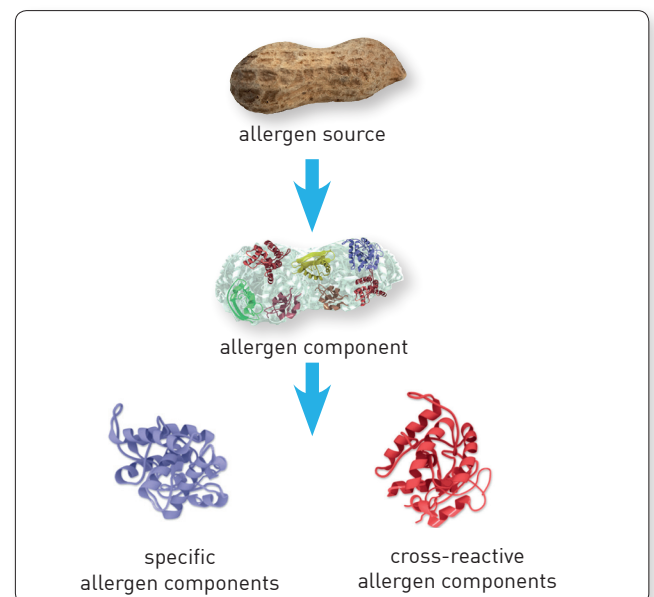


Fig. 2 Any source of allergens is composed of different specific and cross-reactive allergen components. During the ISAC, they are evaluated individually and separately.

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Tab. 1 Protein groups most frequently involved in allergies and their characteristics

(+ low, ++++ high marked)

Protein group	Risk of anaphylactic reactions	Heat and digestion resistant	Cross-reactivity	Example
Storage proteins	++++	++++	+	Ara h 1,2,3,6 (Peanut) Cor a 9 (Hazelnut) Jug r 1,2 (Walnut)
Lipid transfer proteins	+++	+++	++	Ara h 9 (Peanut) Pru p 3 (Peach) Jug r 3 (Walnut)
PR-10 protein	++	++	+++	Bet v 1 (Birch) Gly m 4 (Soy Bean) Pru p 1 (Peach)
Profilins	+	+	++++	Bet v 2 (Birch) Phl p 12 (Timothy grass) Hev b 8 (Latex)

Advantages of the ISAC IgE Allergen Profile in comparison to specific IgE Diagnostics or Prick Test

1. Differentiation between real sensitizations and cross-reactions in order to assess the risk of anaphylactic reactions and for optimal treatment planning.
2. In cases of poly-sensitizations, it facilitates a comprehensive single stage assessment of the sensitization's pattern.

Material

200 µl serum (whole blood)

Request: **ISAC IgE allergen profile**

Costs

Costs for the test are 262.30 €.

Literature

1. Allergen microarrays: a novel tool for high-resolution IgE profiling in adults with atopic dermatitis Ott H. et al. European Journal of Dermatology, 2010, 20, 1-8
2. The ImmunoCAP ISAC molecular allergology approach in adult multi-sensitized Italian patients with respiratory symptoms. Melioli G et al. Clin Biochem 2011, 44, 1005-11
3. A new tool in the field of in-vitro diagnosis of allergy: preliminary results in the comparison of ImmunoCAP 250 with the ImmunoCap ISAC, Gadisseur R et al. Clin Chem Lab Med 2011, 49, 277-280

The results for all allergens are presented in a commented medical report.



Fig. 3 In this detailed commented report, species-specific positive allergen components are listed in the first part, followed by cross-reactive components and a comprehensive comment. In the second part, the results are listed individually according to their respective protein groups.

Tab. 2 ImmunoCap®ISAC Allergen components

Allergen components	Latin Name	Allergen Component	Protein Group
Food Allergens			
Egg white	<i>Gallus Domesticus</i>	nGal d 1 nGal d 2 nGal d 3 nGal d 5	Ovomucoid Ovalbumin Conalbumin/Ovotransferrin Livetin/Serum albumin
Egg yolk/Chicken meat			
Cow's milk	<i>Bos domesticus</i>	nBos d 4 nBos d 5 nBos d 8 nBos d lactoferrin nBos d 6	Alpha-Lactalbumin Beta-Lactoglobulin Casein Transferrin Serum albumin
Cow's milk / beef			
Cod	<i>Gadus callarias</i>	rGad c 1	Parvalbumin
Shrimp	<i>Penaeus monodon</i>	nPen m 1 nPen m 2 nPen m 4	Parvalbumin Arginin kinase Sarcoplasmatic calcium binding protein
Cashew nut	<i>Anacardium occidentale</i>	rAna o 2	Storage protein, 11S Globulin
Brazil nut	<i>Bertholletia excelsa</i>	rBer e 1	Storage protein, 2S Albumin
Hazelnut	<i>Corylus avellana</i>	rCor a 1.0401 rCor a 8 nCor a 9	PR-10 protein Lipid transfer protein (nsLTP) Storage protein, 11S Globulin
Walnut	<i>Juglans regia</i>	rJug r 1 nJug r 2 nJug r 3	Storage protein, 2S Albumin Storage protein, 7S Globulin Lipid transfer protein (nsLTP)
Sesame	<i>Sesamum indicum</i>	nSes i 1	Storage protein, 2S Albumin
Peanut	<i>Arachis hypogaea</i>	rAra h 1 rAra h 2 rAra h 3 nAra h 6 rAra h 8 rAra h 9	Storage protein, 7S Globulin Storage protein, 2S Albumin Storage protein, 11S Globulin Speicherprotein, 2S Albumin PR-10 Protein Lipid transfer protein (nsLTP)
Soy bean	<i>Glycine max</i>	rGly m 4 rGly m 5 rGly m 6	PR-10 protein Storage protein, 7S Globulin Storage protein, 11S Globulin
Buck wheat	<i>Fagopyrum esculentum</i>	nFag e 2	Storage protein, 2S Albumin
Wheat	<i>Triticum aestivum</i>	rTri a 14 rTri a 19.0101 nTri a A_TI	Lipid transfer protein (nsLTP) Omega-5 Gliadin Alpha-Amylase / Trypsin inhibitor
Kiwi	<i>Actinidia deliciosa</i>	nAct d 1 nAct d 2 nAct d 5 rAct d 8	Cystein protease Thaumatococcal protein Kiwellin PR-10 protein
Celery	<i>Apium graveolens</i>	rApi g 1	PR-10 protein
Apple	<i>Malus domestica</i>	rMal d 1	PR-10 protein
Peach	<i>Prunus persica</i>	rPru p 1 rPru p 3	PR-10 protein Lipid transfer protein (nsLTP)
Aeroallergens			
Bermuda grass	<i>Cynodon dactylon</i>	nCyn d 1	Grass, group 1
Timothy grass	<i>Phleum pratense</i>	rPhl p 1 rPhl p 2 nPhl p 4 rPhl p 5 rPhl p 6 rPhl p 7 rPhl p 11 rPhl p 12	Grass, group 1 Grass, group 2/3 Berberine bridge enzyme Grass, group 5 Grass, group 6 Polcalcin Ole e 1- related protein Profilin
Alder	<i>Alnus glutinosa</i>	rAln g 1	PR-10 protein
Birch	<i>Betula verrucosa</i>	rBet v 1 rBet v 2 rBet v 4	PR-10 protein Profilin Polcalcin
Hazel pollen	<i>Corylus avellana</i>	rCor a 1.0101	PR-10 protein
Japanese red-cedar	<i>Cryptomeria japonica</i>	nCry j 1	Pectat lyase
Arizona cypress	<i>Cupressus arizonica</i>	nCup a 1	Pectat lyase
Olive tree	<i>Olea europaea</i>	rOle e 1 nOle e 7 rOle e 9	Olive, group 5 Lipid transfer protein (nsLTP) 1,3-beta-glucanase

Allergen components	Latin Name	Allergen Component	Protein Group
Aeroallergens			
Sycamore tree	<i>Platanus acerifoli</i>	rPla a 1 nPla a 2 rPla a 3	Invertase inhibitor Polygalacturonase Lipid transfer protein (nsLTP)
Common ragweed	<i>Ambrosia artemisiifolia</i>	nAmb a 1	Pectat lyase
Mugwort	<i>Artemisia vulgaris</i>	nArt v 1 nArt v 3	Defensin-like protein Lipid transfer protein (nsLTP)
White goosefoot	<i>Chenopodium album</i>	rChe a 1	Ole e 1-related protein
Annual mercury	<i>Mercurialis annua</i>	rMer a 1	Profilin
Apreading pellitory	<i>Parietaria judaica</i>	rPar j 2	Lipid transfer protein (nsLTP)
English plantain	<i>Plantago lanceolata</i>	rPla l 1	Ole e 1-related protein
Prickly saltwor	<i>Salsola kali</i>	nSal k 1	Pektin methylesterase
Dog	<i>Canis familiaris</i>	rCan f 1 rCan f 2 nCan f 3 rCan f 5	Lipocalin Lipocalin Serum albumin Arginin esterase
Horse	<i>Equus caballus</i>	rEqu c 1 nEqu c 3	Lipocalin Serum albumin
Cat	<i>Felis domesticus</i>	rFel d 1 rFel d 2 rFel d 4	Uterogloblin Serum albumin Lipocalin
Mouse	<i>Mus musculus</i>	nMus m 1	Lipocalin
Mould	<i>Alternaria alternata</i>	rAlt a 1 rAlt a 6	Saures glykoprotein Enolase
	<i>Aspergillus fumigatus</i>	rAsp f 1 rAsp f 3 rAsp f 6	Mitogillin family Peroxysoales protein Mn-superoxid dismutase
	<i>Cladosporium herbarum</i>	rCla h 8	Mannitol dehydrogenase
Dust mite	<i>Blomia tropicalis</i>	rBlo t 5	Mites, group 5
	<i>Dermatophagoides farinae</i>	nDer f 1 rDer f 2	Cystein protease NPC2 family
	<i>Dermatophagoides pteronyssinus</i>	nDer p 1 rDer p 2 rDer p 10	Cystein protease NPC2 family Tropomyosin
Storage mite	<i>Lepidoglyphus destructor</i>	rLep d 2	NPC2 family
German cockroach	<i>Blattella germanica</i>	rBla g 1 rBla g 2 rBla g 5 nBla g 7	Cockroach, group 1 Aspartat protease Glutathion S-transferase Tropomyosin
Other			
Bee venom	<i>Apis mellifera</i>	rApi m 1 nApi m 4	Phospholipase A2 Melittin
Paper wasp venom	<i>Polistes dominulus</i>	rPol d 5	Antigen 5
Wasp venom	<i>Vespula vulgaris</i>	rVes v 5	Antigen 5
Herring worm	<i>Anisakis simplex</i>	rAni s 1 rAni s 3	Serin protease inhibitor Tropomyosin
Latex	<i>Hevea brasiliensis</i>	rHev b 1 rHev b 3 rHev b 5 rHev b 6.01 rHev b 8	Rubber elongation factor Small rubber particle protein Acidic protein Prohevein Profilin
Carbohydrate chains of bromelain		nMUXF3	CCD marker