Laboratoire CERBA

Bio News

ImmunoCAP® ISAC

New development

IN PRATICE…

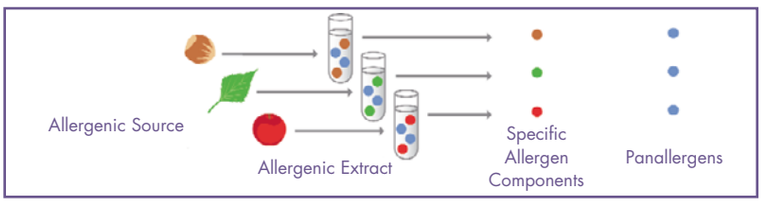
- *SAMPLING:* *0.5 mL of serum or plasma in EDTA*
- *RUN FREQUENCY: twice monthly*
- *TURNAROUND TIME: 1 day*

A new serum test for exploration of polysensitised individuals

Allergy is a major public health issue and its prevalence has doubled in recent years, as a result of which it was recently listed by the WHO as the fourth most common form of disease worldwide. Today, almost one in three people suffer from allergy, and this figure could be as high as one in two by 2010.

Diagnosis

In the presence of signs suggesting allergy, the allergologist plays a key role in identifying the causative substances and determining their responsibility in the onset of symptoms. Allergological diagnosis is based upon careful questioning and skin tests, to which may be added specific IgE assay. Diagnosis may result in the introduction of desensitisation treatment (specific immunotherapy) or withdrawal of the incriminated allergen. It is therefore essential to identify the causative allergens accurately. More than 500 allergen sources are available for specific IgE assay using ImmunoCAP® technology.



In addition to these **allergenic sources**, a further 60 native or recombinant allergens are available, allowing screening for the specific IgE of the individual components of certain sources.

The **allergenic extracts** used in the majority of specific IgE assays and for skin tests are obtained from an **allergenic source**, a raw starting material comprising a heterogeneous mixture of allergenic and non-allergenic substances (proteins or glycoproteins). Assay of the specific IgE of individual substances rather than allergenic extracts is to allow differentiation of specific IgE at the molecular level: certain substances are **specific** for the allergenic source and are thus markers of true sensitisation, while others are substances **common** to many plant pollens and substances of plant origin and are known as **panallergens**, such as profilins for example. Sensitisation to panallergens results in positive skin tests and specific IgE for many allergenic extracts, which does not allow accurate identification of the actual allergenic substance associated with the allergic symptoms in question. These substances are designated using a nomenclature comprising the first three letters of the genus followed by the first letter of the species and a figure indicating the chronological order of purification.

For example, for Timothy pollen (Phleum pratense), rPhl p 1, r Phl p 2, rPhl p 5b, rPhl p 12 indicate recombinant substances while nPhl p 4 refers to the natural substance.

At present, native allergenic substances (isolated by purification) and recombinant allergenic substances (produced by genetic recombination) are available in standard IgE ImmunoCAP® assay. These allow more accurate specific IgE assay at the molecular level since individual patients allergic to a particular allergenic source develop their own specific sensitisation profiles with regard to allergenic substances.

For instance, for patients sensitised to birch pollen, the therapeutic approach differs according to the patient's IgE reactivity profile with regard to Bet v 1 (a marker for true sensitivity) and Bet v 2 + Bet v 4 (cross-reactivity markers).

The ImmunoCAP® ISAC test, which uses innovative **protein biochip** technology, determines specific IgE for 103 allergenic substances obtained from 40 different allergenic sources.

The ImmunoCAP® ISAC may be used to improve the investigation of patients developing a complex sensitisation profile (e.g. polysensitised patients), analysis of which requires screening for IgE specific for a wide range of substances. It can be used to optimise therapy thanks to applications that are now currently used in molecular diagnosis of allergy:

- ✓ differentiation between specific sensitisation and cross-reactivity in order to better target specific therapy (immunotherapy, withdrawal).
- ✓ determination of the severity of reaction.

The 103 allergenic substances in question have been selected so as to cover a wide range of allergens: tree pollens, grasses, weeds, mites, animal danders, moulds, latex, foods and insect venoms. A calibration serum is used to provide quantitative results expressed in ISU (ISAC Standardized Units).

The results are classified under two headings:

- ✓ by protein group (specific markers for species, markers of cross reactivity), accompanied by notes indicating the role played by cross-reactivity markers in symptoms.
- ✓ by allergen source, with details for each of the specific IgEs of the various different components.

ImmunoCAP® ISAC allows a complete IgE reactivity profile to be established, which is especially useful to distinguish specific markers for species and panallergens responsible for cross-reactivity and rarely incriminated in symptoms. This test therefore provides new diagnostic information and allows improved management of polysensitised patients.

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ImmunoCAP® ISAC test: allergenic compounds by protein family

		Family	Allergenic source	Allergenic substances	Role
PLANTS	**Markers for true sensitisation**		Timothy	**Phl p 1, Phl p 2, Phl p 4, Phl p 5, Phl p 6, Phl p 11**	Major allergens.
			Olive	**Ole e 1**	
			Plane tree	Pla a 1, Pla a 2	
			Bermuda grass	**Cyn d 1**	
			Cypress	Cup a 1	
			Ragweed	**Amb a 1**	
			Mugwort	**Art v 1**	
			Japanese Ceder	Cry j 1	
			Cypress	Cup a 1	
			Saltwort	Sal k 1	
			Peanut	**Ara h 2, Ara h 1, Ara h 3**	
			Hazelnut	Cor a 9	
			Brazil Nut	**Ber e 1**	
			Cashew nut	Ana o 2	
			Sesame seed	Ses i 1	
			Kiwi	Act d 1, Act d 2, Act d 5	
			Soybean	Gly m glycinin, Gly m β-conglycinin	
			Wheat	Tri a 18, Tri a gliadin, **Tri a 19.0101**	
			Latex	**Hev b 1, Hev b 3, Hev b 5, Hev b 6**	
	Markers for cross-reactivity	PR-10 protein, Bet v 1 homologue	Birch	**Bet v 1**	Allergy to birch pollen, common in Northern and Central Europe, is often associated with oral syndromes, in relation with PR10, a heat-sensitive protein found in raw fruit and vegetables. These foods are tolerated if cooked.
			Alder	Aln g 1	
			Hazelnut	Cor a 1.0401	
			Hazel pollen	Cor a 1.0101	
			Apple	Mal d 1	
			Peach	**Pru p 1**	
			Soybean	**Gly m 4**	
			Peanut	**Ara h 8**	
			Celery	**Api g 1**	
			Carrot	Dau c 1	
			Kiwi	Act d 8	
		LTP (non-specific Lipid Transfer Protein, nsLTP)	Peach	**Pru p 3**	LTPs are resistant to heat and enzymatic hydrolysis. They cause severe systemic allergic reactions, even if the fruit in question is cooked. Such reactions are most commonly observed in southern Europe.
			Hazelnut	**Cor a 8**	
			Mugwort	Art v 3	
			Wall pellitory	**Par j 2**	
		Profilin	Birch	**Bet v 2**	Panallergen responsible for broad cross-reactivity between plants. Responsible for fairly moderate symptoms but in rare cases, sever reactions have been seen.
			Olive	Ole e 2	
			Latex	**Hev b 8**	
			Annual mercury	Mer a 1	
			Timothy	**Phl p 12**	
		Storage protein	Birch	**Bet v 4**	Structural protein, a panallergen responsible for broad cross-reactivity between plants, but only rarely associated with symptoms.
			Timothy	**Phl p 7**	
		CCD (Cross-reactive Carbohydrate Determinants)	Bromelin	Ana c 2	Marker for cross-reactivity associated with carbohydrate determinants of pollens, foods of plant origin, latex, venom.
OTHER	**Species-specific markers**		Egg	**Gal d 1** (ovomucoid), **Gal d 2** (ovalbumin), **Gal d 3** (conalbumin)	Major allergens.
			Milk	**Bos d 4 (alpha-lactalbumin, Bos d 5 (beta-lactoglobulin) Bos d 8 (caseins) Bos d lactoferrin (transferrin)**	
			Cockroach	Bla g 1, Bla g 2, Bla g 4, Bla g 5	
			Cat	**Fel d 1**, Fel d 4	
			Dog	**Can f 1, Can f 2**	
			Mouse	Mus m 1	
			Alternaria	**Alt a 1**, Alt a 6	
			Aspergillus	**Asp f 1, Asp f 2, Asp f 3, Asp f 4, Asp f 6**	
			Cladosporium	Cla h 8	
			Anisakis	Ani s 1	
			Honey bee venon	Api m 1, Api m 4	
	Markers for cross-reactivity limited to family	Protease cystein	House dust mite	Der p 1, Der f 1	Allergens responsible for broad cross-reactivity between the different species of this family.
		NPC2	House dust mite	Der f 2, Der p 2, Eur m 2	
	Markers for cross reactivity	Parvalbumin	Carp	**Cyp c 1**	Major fish allergen, allergy marker, stable to heat.
			Cod	**Gad c 1**	
		Tropomyosin	Shrimp	**Pen a 1**, Pen i 1, Pen m 1	Protein in muscle fibres, marker for cross-reactivity between crustaceans, mites and cockroach.
			House dust mite	Der p 10	
			Cockroach	Bla g 7	
			Anisakis	Ani s 3	
		Serum albumin	BSA	Bos d 6	Protein found in the tissue of different animals (beef, chicken), eggs, cows milk, accounting for cross reaction between albumin from different animal species (e.g. cat/dog, cat/pig).
			Cat	Fel d 2	
			Dog	Can f 3	
			Horse	Equ c 3	
			LSA (livetin)	Gal d5	

In bold: allergenic substances available for individual assay of specific IgE using ImmunoCAP®