EUROIMMUN Medizinische Labordiagnostika AG

DPA-Dx* Insect Venoms

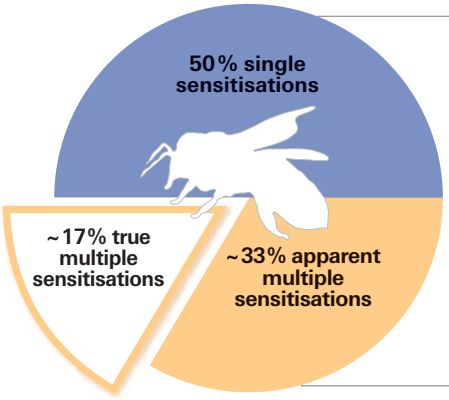
Modern diagnostics for the differentiation of insect venom allergies

- **Precise identification of insect venom sensitisations**
- **Differentiation of cross reactions and unspecific CCD** reactions**
- **Selection of suitable specific immunotherapy (SIT)**

* Allergy diagnostics by means of defined partial allergens
** Cross-reactive carbohydrate determinants

Insect venom allergies...

- are more frequently caused by stings from bees and wasps, less frequently by paper wasps and hornets.
- affect 9.2–28.7% of the population[1].
- may develop independently of age and even after many asymptomatic contacts.
- lead to systemic reactions in 0.3–7.5% of allergic persons (e.g. itching, angiooedema, breathing difficulties, lightheadedness, low blood pressure, bradycardia, heart arrhythmia, nausea)[2].
- affect quality of life, since the patients are required to carry an epinephrine autoinjector at all times.
- can be effectively treated by means of specific immunotherapy for hyposensitisation.



50% of persons who are allergic to insect venom are sensitised to one venom. The other half show reactions to several insect venoms, although only around 17% of the affected individuals are actually multiply sensitised[3, 4]. In the other cases, cross-reactions are present, which are due to related allergens of the different insect species or unspecific carbohydrate determinants (CCD).

Defined partial allergen diagnostics (DPA-Dx)

In conventional allergy diagnostics, insect venom extracts are used for the detection of specific IgE (sIgE) against the allergen source. These extracts are a mix of different proteins, of which some (allergen components), but not all, have allergenic potential.

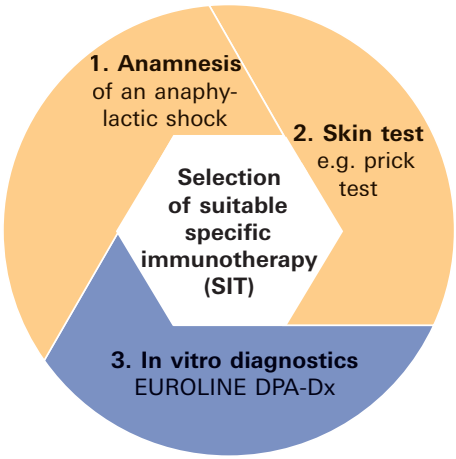
In contrast, defined partial allergen diagnostics (DPA-Dx) employ **individual allergen components** which are extracted from the allergen source or recombinantly produced. This method offers many advantages:

1. Standardisation	The allergen composition of extracts may vary. Standardised production of partial allergens is possible (native and recombinant).
2. Sensitivity	Partial allergens which are naturally underrepresented in the extract can be recombinantly produced and tested.
3. Cross reactivity	DPA-Dx allows differentiation between cross reactions and true sensitisations. Moreover, the recombinant allergens are free from CCD and therefore enable the exclusion of unspecific CCD reactions, in contrast to extracts.
4. Stability	Individual native components may show a low stability and degrade in the extract. Recombinant partial allergens are stable.

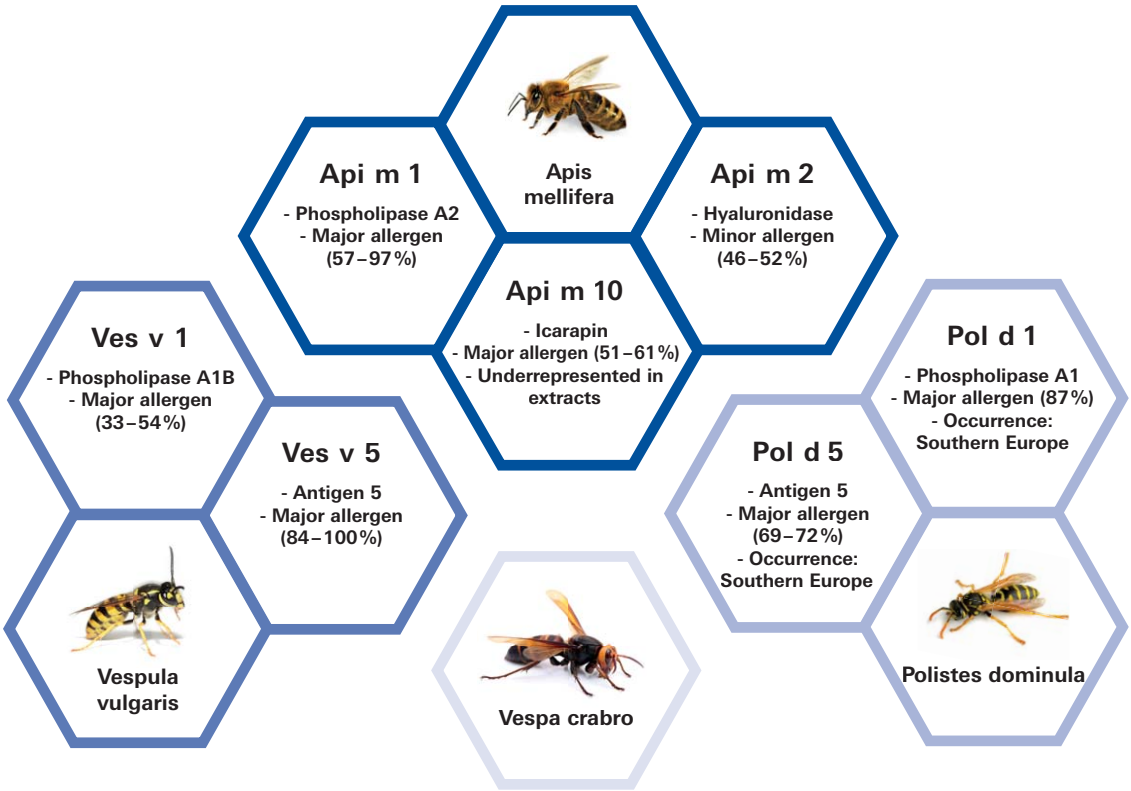
Methods to decide on suitable specific immunotherapy

Hyposensitisation (specific immunotherapy, SIT) is an important option of causal treatment of an allergy. In order for the SIT to be successful, an individually suited medication containing a sufficient amount of the allergen component which the patient is sensitised to must be applied.

If an insect venom allergy is suspected after anamnesis and a skin test, DPA-Dx allows precise determination of the allergy-causing components. Based on the three diagnostic methods, the medication suited for the patient can be selected.



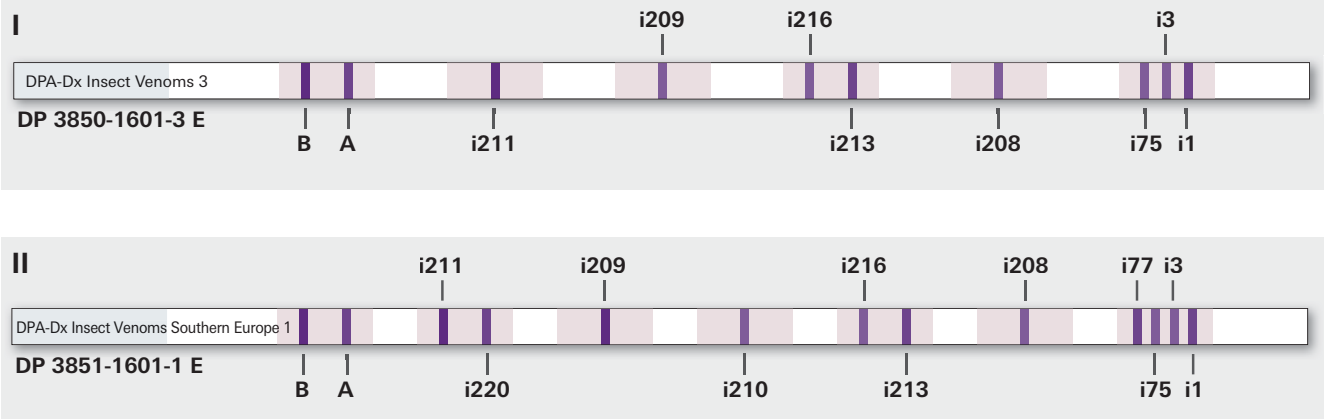
Multiparameter insect venom allergy profiles from EUROIMMUN



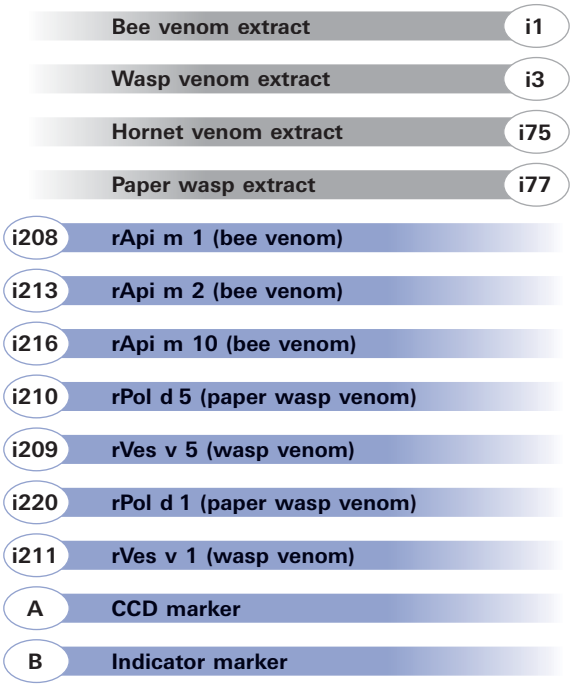
Combination of insect-specific venom components and extracts

EUROLINE Insect Venom Profiles enable differentiation between sensitisations against insect venoms of different Hymenoptera species, such as bee (Apis mellifera), wasp (Vespula vulgaris), paper wasp (Polistes dominula) and hornet (Vespa crabro). The multiparameter system allows for comprehensive diagnostics in one incubation. The use of partial allergens increases the analytical specificity and sensitivity.

EUROLINE DPA-Dx Insect Venoms



- Clear identification of a sensitisation to bee, wasp (I), hornet (II) and/or paper wasp (III)
- Api m 1 and Api m 10 cover > 87 % of bee venom sensitisations; Api m 10 is underrepresented in extracts.
- Ves v 1 and Ves v 5 cover > 95 % of wasp venom sensitisations.
- Pol d 1 and Pol d 5 cover ~ 100 % of paper wasp venom sensitisations; complemented by Pol d 1 for increased diagnostic sensitivity.[5]
- Marker for the detection of sIgE against CCD structures



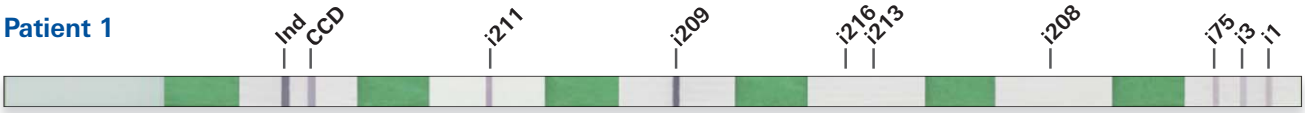
Correlation data: Agreement of EUROLINE DPA-Dx Insect Venoms 2 and ImmunoCAP[6]

Bee venom extract	85 %
rApi m 1 (bee venom)	96 %
Wasp venom extract	93 %
rVes v 5 (wasp venom)	96 %
rVes v 1 (wasp venom)	86 %

Case examples of insect venom allergies

Two patients show allergic reactions to insect bites. In both cases, the extract-based analysis indicates a multiple sensitisation to bee, wasp and hornet venoms (i1, i3, i75). The allergy-causing insect venom is identified through defined partial allergen diagnostics.

Patient 1



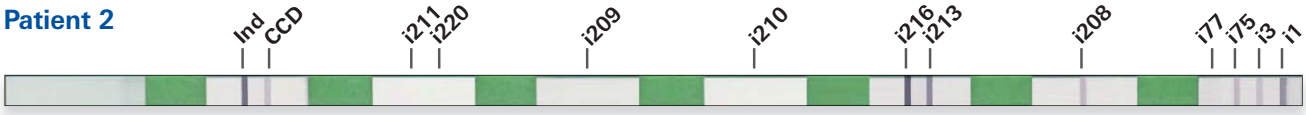
EUROLINE DPA-Dx Insect Venoms 3 (DP 3850-3):

Result with defined partial allergen diagnostics: → **Conclusion:**

Additionally to the extracts from bee, wasp, and hornet venom, also the CCD marker and the wasp venom partial allergens Ves v 1 (i211) and Ves v 5 (i209) yield positive signals.

The analysis detects IgE against CCD, which may be responsible for an apparent multiple sensitisation. The CCD-free partial allergens of the EUROLINE demonstrate that only a single sensitisation against wasp venom is present.

Patient 2



EUROLINE DPA-Dx Insect Venoms Southern Europe 1 (DP 3851-1)

Results with defined partial allergen diagnostics: → **Conclusion:**

The extracts from bee, wasp and hornet venom, as well as the CCD marker and the bee venom partial allergens Api m 1 (i208), Api m 2 (i213) and Api m 10 (i216) show positive signals.

The analysis detects IgE against CCD which may be responsible for an apparent multiple sensitisation. The CCD-free partial allergens of the EUROLINE demonstrate that only a single sensitisation against bee venom is present.

Advantages of DPA-Dx Insect Venom Profiles for diagnostics of insect venom allergies

- Estimation of the risk of severe allergic reactions
- Detection of sensitisations against specific insect venom components
- Differentiation between cross reactions and multiple sensitisations
- Selection of suitable immunotherapy
- Only small amounts of serum (100 – 400 µl) required – ideal for paediatrics
- From sample to result report in less than 3.5 hours
- Individual automation solutions
- Standardised evaluation according to EAST (enzyme allergo sorbent test)-class system with the EUROLineScan software.

[1] *Bilo BM, et al. Diagnosis of hymenoptera venom allergy. Allergy 60:1339-1349 (2005).*
[2] *Schiener M, et al. Allergen-specific immunotherapy of hymenoptera venom allergy – also a matter of diagnosis. Hum Vaccin Immunother 13(10):2467-2481 (2017).*
[3] *Spillner E, et al. Hymenoptera allergens: from venom to „venome". Front Immunol 5:77 (2014).*
[4] *Reisman RE, et al. Further studies of patients with both honeybee- and yellow-jacket-venom-specific IgE. Int Arch Allergy Appl Immunol 82(2):190-194 (1987).*
[5] *Bilò MB, et al. Prevalence of Pol d 1 sensitization in Polistes dominula allergy and its diagnostic role in vespid double-positivity. J Allergy Clin Immunol Pract 16: S2213-2198(21)00660-7 (2021).*
[6] *Micaletto S, et al. Comparison of two methods for measuring IgE to a panel of partly molecular based hymenoptera allergens. Poster presentation at EACCI Congress (2016).*