ImmunoCAP venom components help improve diagnosis of

venom allergy

VENOM ALLERGY

ImmunoCAP® ALLERGEN COMPONENTS

Hymenoptera venom allergies

Allergy to Hymenoptera venoms (HVA) is one of the most frequent causes of anaphylaxis in adults. The self-reported prevalence of systemic reactions to HV is in the range of 0.3 % to 7.5 % in the general population and as high as 14–43 % among beekeepers.[1] An important risk factor for severe reactions to HV is elevated base line serum tryptase levels, such as in mastocytosis patients.[1–3]

VIT treatment – importance of a correct diagnosis

Venom immunotherapy (VIT) is effective for treating patients with severe HV allergy, inducing tolerance in 75–98 % of patients.[4] Patients selected for VIT are diagnosed based on a medical history of systemic sting reactions and a positive test for venom sensitization.[1, 5] Since HV allergic patients may have very low levels of venom specific IgE, tests of the highest possible sensitivity are required.

VIT treatment outcome is dependent on correctly identifying the insect to which the patient is allergic and selecting the corresponding venom for immunotherapy. Due to difficulties in identifying the culprit insect at the time of the sting and confounding factors causing double positivity to honey bee and wasp venoms, uncertainty is common. At the same time, unnecessary treatment with both bee and wasp venoms represents an increased risk of side effects as well as higher costs and is therefore undesirable.[4]

Commercially available therapeutic venom preparations used for VIT have been shown to differ in their content of important allergens[6, 7] which may have implications for the treatment success. Identification of patients with dominant sensitization to allergens poorly represented in certain therapeutic venom preparations may therefore serve to guide the choice of optimal treatment.[8]

Resolving double positivity with CCD free allergen components

As many as 50 % of HV allergic patients show IgE reactivity to both honey bee and wasp venoms.[4] While such double positivity may in some cases be due to true double sensitization or reflect cross-reactivity between structurally related bee and wasp venom proteins, it is more often caused by the presence of IgE antibodies recognizing cross-reactive carbohydrate determinants (CCD) present on both bee and wasp venom proteins.[4, 9]

Given that patients are often unable to unambiguously identify the insect by which they were stung diagnosis with traditional tools often remains incomplete in cases of double test positivity. Fortunately, many of these cases can be effectively resolved using tests based on CCD free recombinant venom allergen components.[10] As a result, a more correct diagnosis can be made in regard to identification of the culprit insect and adequate treatment provided.

Helping to fill the gaps in HVA diagnostics

At least 95 % of wasp venom allergic patients are sensitized to either or both of the two major wasp venom components Ves v 1 and Ves v 5.[11, 12] In contrast, bee venom allergy is considerably more complex with patients showing a more variable pattern of sensitization to a greater number of relevant allergen components.[7, 13, 14] Api m 1 is the major allergen in honey bee venom both in terms of sensitization frequency and abundance in honey bee venom. However, recent studies indicate a population or geography related frequency of Api m 1 sensitization among bee venom allergic patiens, ranging between 55 and 80 %.[7, 13-17]

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To help improve the clinical diagnosis of HV allergic patients, a broad range of HV components are available as ImmunoCAP tests (Table 1). By enabling quantitative measurement of IgE antibodies to individual CCD free recombinant venom allergens, ImmunoCAP allergen components can help resolve double positivity to bee and wasp venoms and fill a gap in the diagnosis of HV allergy.

In addition to Api m 1, the bee venom components Api m 2, Api m 3, Api m 5 and Api m 10 are all relevant allergens to which bee venom allergic patients show a highly variable sensitization profile.[7] Together with Api m 1, a combined diagnostic sensitivity of 93 % was recently demonstrated and, importantly, they were found to detect 75 % of patients not sensitized to Api m 1.[7] Although Api m 4 represents as much as 50 % of the dry weight of honey bee venom and therefor might be considered a potentially important allergen, recent studies suggest that it is of limited clinical significance.[4,7]

Api m 3 and Api m 10 – proteins unique to bee venom

Api m 3 (acid phosphatase) and Api m 10 (icarapin) are bee venom allergens belonging to protein families that are not represented in wasp venoms. Thus, these components are undisputable markers of primary bee venom sensitization.[18,19]

Up to two thirds of patients with a history of anaphylaxis to honey bee venom are sensitized to Api m 3 and/or Api m 10 and in a recent study, 5 % of the subjects were exclusively reactive to either or both of these two components.[18,19] These observations are of particular importance as Api m 3 and Api m 10 have both been shown to be underrepresented or even undetectable in therapeutic bee venom preparations.[6,7,23] Patients with a dominant sensitization to Api m 3 and/or Api m 10 may be at risk of not obtaining the protection intended by VIT treatment.[8,23]

Api m 2 and Api m 5 – primarily indicative of bee venom sensitization

A considerable proportion of bee venom allergic patients show sensitization to Api m 2 (hyaluronidase) and Api m 5 (dipeptidyl peptidase).[7,17] Forty percent or more of patients negative to Api m 1 but with a history of bee venom induced reactions showed sensitization to Api m 2 and Api m 5, respectively.[7] Proteins belonging to the same protein families as Api m 2 and Api m 5 are present in wasp venoms and designated Ves v 2 and Ves v 3, respectively. However, with no more than 46–55 % amino acid sequence identity between the bee and wasp venom proteins, only a limited level of cross-reactivity can be expected.[20,21] Further, disregarding CCD-reactivity, sensitization to Ves v 2 appears to occur rarely among wasp venom allergic subjects.[20–22] Similarly, Ves v 3 does not appear to be an important determinant in wasp venom allergy.

Honey bee	Common/ Paper wasp	Tryptase
rApi m 1 (i208)	rVes v 1 (i211)	
rApi m 2 (i214)	rVes v 5 (i209)	
rApi m 3 (i215)	rPol d 5 (i210)	
rApi m 5 (i216)		
rApi m 10 (i217)		

Table 1. Tools to aid in HVA diagnostics: ImmunoCAP venom components and ImmunoCAP Tryptase.

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