

Letter to the Editor

***Polistes* species venom is devoid of carbohydrate-based cross-reactivity and allows interference-free diagnostics**

To the Editor:

Allergy to venom of paper wasps (*Polistinae*) is common in North America as well as in Europe, especially in Mediterranean areas. The most important *Polistes* species in Europe are *P. dominula* and *P. gallicus*, whereas in Northern America other species such as *P. annularis*, *P. apachus*, *P. exclamans*, *P. fuscatus*, and *P. metricus* are dominant. In the last few decades, *P. dominula* has increasingly spread across the North American continent and the central and northern parts of Europe. This phenomenon has been suggested to be associated with environmental changes, explaining the increasing importance of *Polistes* venom allergy as a cause for anaphylactic Hymenoptera sting reactions. A lack of molecular tools and the neglect of specific diagnosis in northern regions classically dominated by other Hymenoptera such as yellow jackets and honeybees are likely to additionally contribute to underestimating *Polistes* venom (PV) allergy.^{1,2}

Diagnosis of Hymenoptera venom allergy is based on a history of anaphylactic sting reactions, positive skin test responses, and/or detection of specific IgE to Hymenoptera venom. Positive results in skin and serological tests with conventional venom extracts, however, do not always reflect genuine sensitizations but

are frequently caused by clinically irrelevant cross-reactive antibodies. Treatment modalities therefore often include different venoms, resulting in higher costs, increased risk of severe side effects, and possible de novo sensitizations.³

A high percentage of cross-reactivity has been attributed to IgE directed against cross-reactive carbohydrate determinants (CCDs), namely, to α 1,3-linked core fucose residues of glycoproteins. Therefore, molecular diagnosis applying nonglycosylated species-specific allergens and strategies to circumvent α 1,3-core fucosylation led to a significant advance in the dissection of true double sensitization versus irrelevant cross-reactivity.^{4,5}

The molecular cross-reactivity between European and American *Polistes* species is described as rather low because they belong to different subgenera. In contrast, cross-reactivity between *Polistinae* and *Vespinae* (*Vespula*, *Dolichovespula*, and *Vespa*) venoms and purified venom proteins² is frequently observed especially for *Vespula* and American as well as European PV.¹ Moreover, it is widely accepted that IgE cross-reactivity in a significant fraction of patients can be attributed to CCDs.¹

In this study, we addressed for the first time the CCD reactivity of European and American PV. We utilized *Galanthus nivalis* agglutinin, which indicates the general presence of N-linked glycans, and rabbit anti-horseradish peroxidase (HRP) serum that specifically detects α 1,3-core fucosylation⁶ of insect venoms. Applying *Galanthus nivalis* agglutinin in AlaBlots

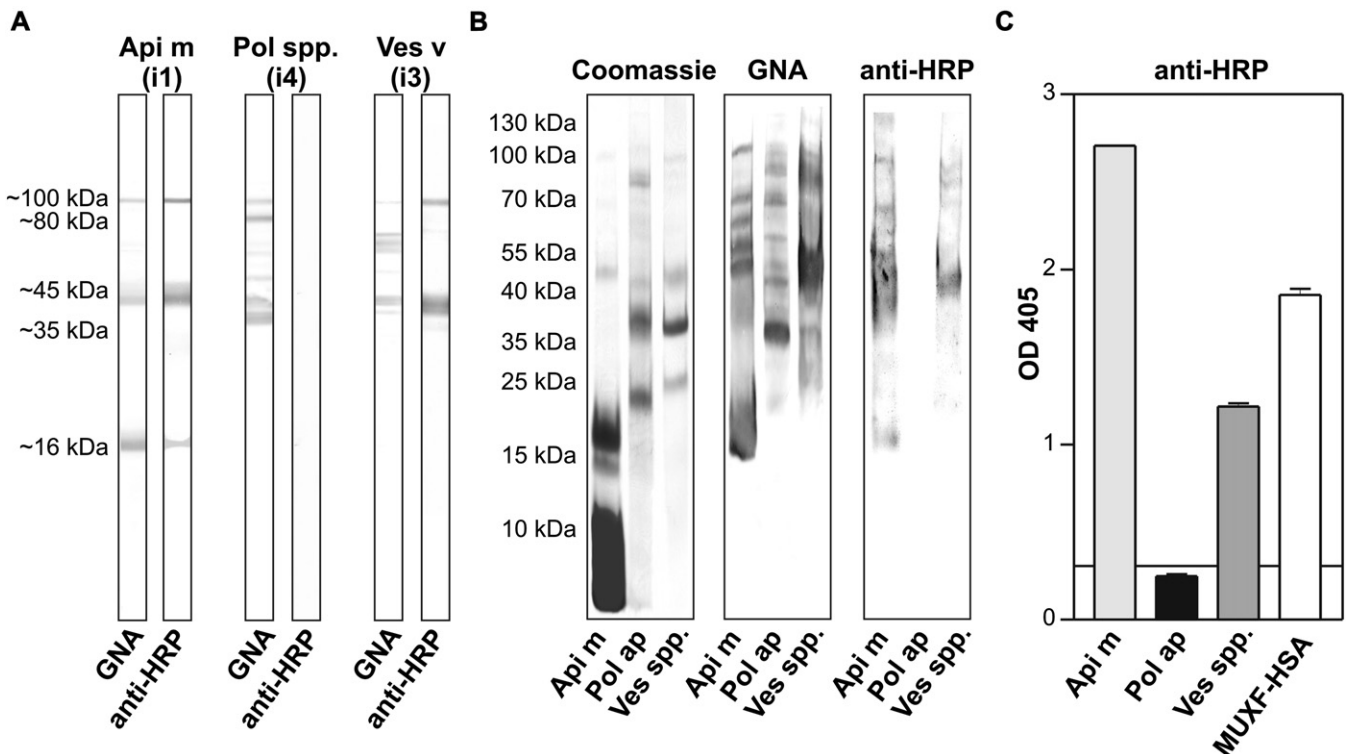
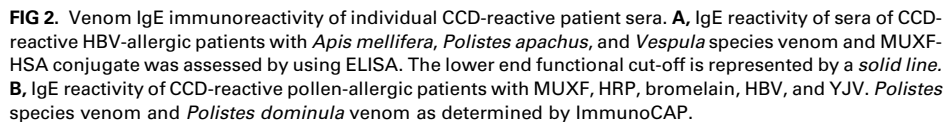


FIG 1. Glycosylation pattern of *Polistes*, *Apis*, and *Vespula* venom preparations. **A**, AlaBlots of *Apis mellifera*, *Polistes* species, and *Vespula vulgaris* venom detected with *Galanthus nivalis* agglutinin indicating the presence of glycosylation or with anti-HRP serum specific for α 1,3-core fucosylation. **B**, SDS-PAGE and immunoblot analysis of *A. mellifera*, *Polistes apachus*, and *Vespa* species venom visualized as above. **C**, ELISA analysis of *A. mellifera*, *P. apachus*, and *Vespa* species venom and MUXF-human serum albumin conjugate by using the anti-HRP serum. GNA, *Galanthus nivalis* agglutinin.



Although facilitated by the lack of CCD-based interference in PV, the discrimination of PV and YJV allergy still remains difficult, and often requires additional laboratory tests (eg, IgE inhibition assays) to distinguish primary sensitization and

protein-based cross-reactivity.¹ These tests are expensive, time consuming, difficult to interpret, and thus rarely used in clinical routine. The availability of CCD-free marker allergens from HBV and YJV has significantly improved the discrimination between primary HBV and YJV sensitization.^{4,8,9} Similarly, the use of phospholipases and antigen 5 has been suggested to facilitate the discrimination between primary PV and YJV sensitization² although the known degree of sequence homology still does not rule out peptide cross-reactivity and thus only allows the estimation of the probable sensitizing venom. Here, clearly additional marker allergens devoid of any cross-reactivity are required that allow us to reliably identify PV allergy and choose the appropriate therapy in all areas in which *Polistes* species are dominant or gain importance.

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