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LETTER



Reply to the letter to the editor concerning the review Immunotherapy for pet allergies

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Reply

I thank Dr. Liccardi and co-authors for the interest in my review article on pet allergen immunotherapy.¹ They raise an important question concerning clinical cases with poor results in dog allergen immunotherapy highlighting the importance of exact clinical allergy diagnosis so that the therapy can be targeted specifically.² Here, as they write, component resolved diagnosis (CRD) can be of great value, as it can help to identify the primary sensitizer. Obviously, if CRD indicates that the subject is sensitized to Can f 1, Can f 2 or Can f 5, which are considered the specific markers of primary sensitization to dog,³ allergen immunotherapy (AIT) should be conducted with a dog allergen extract containing these allergens to obtain the immunological impact. In other words, it is plausible that if the source of primary sensitization is some other animal than dog, *in vitro* IgE cross-reactivity or cross-sensitization interfering with the identification of the culprit, AIT with a dog allergen extract gives a poor result. Formerly, when specific IgE measurements exclusively relied on allergen extracts, instead of single (recombinant) allergen molecules, distinction between primary and cross-sensitization was hard. As the Dr. Liccardi and co-authors indicate, the high quality of dog allergen extracts is instrumental for a successful result in the therapy. Therefore, the commercial producers of allergen extracts for AIT play a decisive role in supplying products that contain all the relevant allergen components.

One important factor which can contribute to the efficacy of dog allergen immunotherapy is the nature of dog allergens. Out of seven dog allergens recognized by WHO/IUIS Allergen Nomenclature Sub-Committee (<http://www.allergen.org>) four are lipocalins which are known to show homology with human proteins.^{4,5} For example, dog Can f 1 which is discussed by Dr. Liccardi and co-authors shows an amino acid identity of about 60% with human lipocalin-1 (von Ebner's gland protein/tear lipocalin). The amino acid identity of Can f 5, prostatic kallikrein, is at the similar level with its human counterparts.⁵ Therefore, these allergens may not be immunogenic enough to produce non-allergenic, regulative response in AIT. It is also conceivable that individuals can differ in this respect. In line with the hypothesis, we have previously shown that lipocalin allergens are poorly immunogenic in a mouse model,^{6,7} weakly

antigenic *in vitro*,^{8–11} and the T-cell epitopes examined in detail are recognized suboptimally by human T cells.^{4,12,13} The frequency of lipocalin allergen-specific CD4+ T cells is very low in the peripheral blood of allergic subjects, at the level of 10^{–5} to 10^{–6} circulating cells,^{11,14–17} whereas the frequency of Can f 5-specific CD4+ T cells appears to be slightly higher.¹⁸ Moreover, lipocalin allergens do not appear to show dendritic cell-activating capacity which can be expected to contribute to their weak immunogenic capacity.¹⁹

In conclusion, CRD associated with AIT conducted with high-quality dog allergen extracts, possibly boosted with single allergenic molecules, or with preparations composed of recombinant allergens, perhaps chosen according to an individual sensitization pattern of a patient, together with novel adjuvants and immunization modes can be anticipated to enhance the treatment of dog allergy in the future.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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