

D. VILLALTA<sup>1</sup>, M. MILANESE<sup>2</sup>, M. DA RE<sup>1</sup>, G. SABATINO<sup>3</sup>, M. SFORZA<sup>4</sup>,  
L. CALZETTA<sup>4,5</sup>, G. LICCARDI<sup>5,6</sup>

## Frequency of allergic sensitization to Can f 5 in North East Italy. An analysis of 1403 ISACs 112 (component resolved diagnosis) collected retrospectively

<sup>1</sup>Immunology and Allergy Unit, Santa Maria degli Angeli Hospital, Pordenone, Italy

<sup>2</sup>Division of Pulmonology, S. Corona Hospital, Pietra Ligure, Italy

<sup>3</sup>Biologist

<sup>4</sup>Department of Experimental Medicine, Unit of Respiratory Medicine, University of Rome "Tor Vergata", Rome, Italy

<sup>5</sup>Postgraduate School of Respiratory Medicine, Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy

<sup>6</sup>Department of Pulmonology, Haematology and Oncology, Division of Pulmonology, Unit of Allergology, High Speciality "A. Cardarelli" Hospital, Naples, Italy

### KEY WORDS

*allergic rhinitis; allergic sensitization; bronchial asthma; Can f 5; component resolved diagnosis, CRD; dog; dog allergy; hypersensitivity*

### Corresponding author

Gennaro Liccardi  
Department of Pulmonology,  
Haematology and Oncology  
Division of Pulmonology and  
Unit of Allergology  
High Speciality "A. Cardarelli"  
Hospital  
Piazzetta Arenella 7, 80128  
Naples, Italy  
Phone : +39 081 747 3335-4-3  
E-mail: gennaro.liccardi@tin.it

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### Summary

*Recent studies have shown the increasing relevance of allergic sensitization to Can f 5, a prostatic kallikrein expressed in the prostate and detectable only in male dogs. The aim of the present study was to establish the frequency, level of sensitization and association with other dog allergens of Can f 5, as assessed by component resolved diagnosis (CRD ISAC 112, ThermoFisher Scientific, Uppsala, Sweden) in North East Italy.*

*A total of 1403 CRD ISAC 112 were examined retrospectively. Five hundred twenty subjects (37%) had a positive IgE response to at least one of the available animal allergens. Among these 520 subjects, 268 (51.5%) showed at least one sensitization to dog allergens. Among dog-sensitized individuals, 183 (69.02%) showed IgE against Can f 5, and 106 (57.92%) were sensitized exclusively against Can f 5. The average Can f 5 specific IgE was 8.810 ISU-E, with 77.6% of individuals showing medium or high values of specific IgE according to manufacturer's specifications.*

*In conclusions, our data confirmed that there is a high number of patients sensitized to Can f 5, which have a high degree of allergic sensitization. These results should be taken into account by allergists managing dog allergic patients. In fact, clinical consequences of this sensitization regard respiratory allergy (burden of rhinitis/asthma), systemic reactions (anaphylaxis during sexual intercourse from cross-reaction with human prostatic antigen), allergen immunotherapy-AIT (likely ineffective in patients with exclusive sensitization), and preventive measures (possibility to own a female dog and a likely reduction of allergen passive transport). Further studies are needed to better explore these aspects in "real life".*

Dog allergens are a common cause of allergic sensitization and triggering respiratory symptoms worldwide, especially in geographical areas characterized by a high level of pet ownership such as US and Northern Europe (1,2). It is well known that common dog allergens belong to lipocalins or albumins families of proteins (3-5).

Can f 5, a newly described dog allergen, is a prostatic kallikrein, an androgen-regulated protein expressed in the prostate and detectable only in male dogs (6). Few studies have shown that the rate of a prevalent or exclusive allergic sensitization to Can f 5 is high, ranging between 37% and 52% in the case of dog

sensitized patients or pet-sensitized individuals living in areas with a high pet ownership (6-8). The peculiar characteristics of Can f 5, in highly or exclusive sensitized patients, can determine positive and negative actions which must be carefully evaluated by allergists managing such patients (9,10).

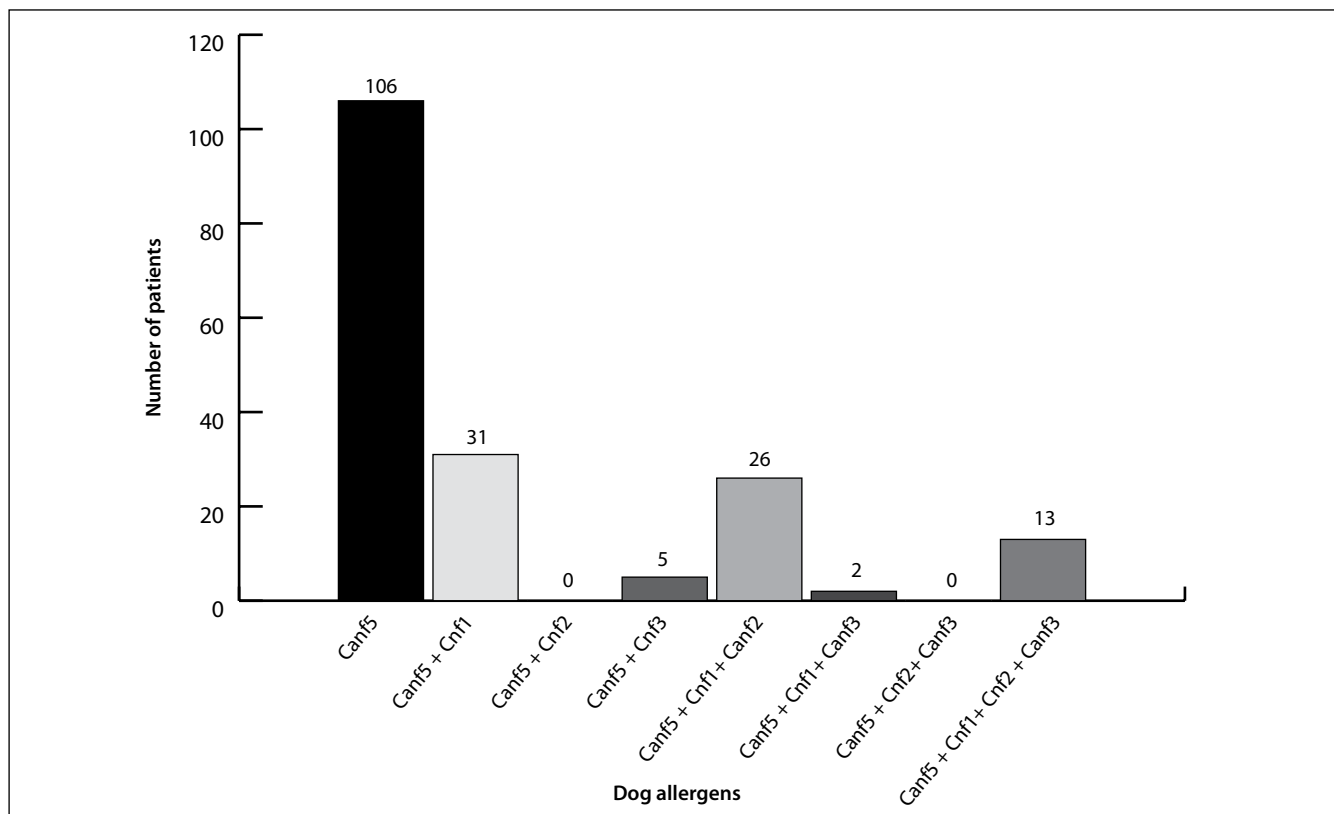
In Italy, data on the frequency of Can f 5 as sensitizing agent in dog allergic individuals are lacking. Therefore, we performed a study in North East Italy to investigate the frequency, the degree of sensitization and the association with other dog allergens, as assessed by Component Resolved Diagnosis (CRD). We retrospectively examined all CRD (ISAC 112, ThermoFisher Scientific, Uppsala, Sweden) carried out from January 1 2013 to December 31 2016 at the Immunology and Allergy Unit of Santa Maria degli Angeli Hospital, Pordenone, Italy. Among CRD results, we have selected those containing IgE against animal allergens including those against dog allergens. The number of individuals with positivity to at least one dog allergen was calculated, as well as the number of Can f 5 sensitizations and average of IgE titration. IgE values were considered as low (0.3 - 0.9 ISU-E), medium (1 - 15 ISU-E) and high (> 15 ISU-E) according to manufacturer's indications.

A total of 1403 consecutive samples from patients with an age range between 4 - 67 years (54% females) were examined with CRD ISAC 112. Five hundred twenty subjects (37%) had a positive IgE response to at least one of available animal allergens (Fel d 1, Fel d 2, Fel d 4, Can f 1, Can f 2, Can f 3, Can f 5, Equ c 3, Mus m 1, Bos d 1). Among these 520 subjects, 268 (51.5%) showed at least one sensitization to allergens of dog. Among dog-sensitized individuals, 183 (69.02%) showed IgE against Can f 5, and 106 (57.92%) were sensitized exclusively to Can f 5.

The association between different dog allergens (Can f 1, Can f 2, Can f 3 and Can f 5) in 183 Can f 5-sensitized patients is described in **figure 1**. The average degree of all 183 sensitizations was 8.810 ISU-E.

The results of our study demonstrated that Can f 5 represents an allergen characterized by high frequency, considering both the number of sensitized individuals (69.02% among 268 dog sensitized ones, and 57.92% as exclusive sensitization) and the level of sensitization (77.6% of individuals showed medium or high values of specific IgE according to manufacturer's specifications). From a general point of view, we believe that the role of Can

**Figure 1** - Association between different dog allergens (Can f 1, Can f 2, Can f 3 and Can f 5) in 183 Can f 5-sensitized patients.



f 5 in dog - allergic individuals might be more multi - faceted than previously reported. The practical consequences regard respiratory allergy (burden of rhinitis/asthma), systemic reactions (anaphylaxis during sexual intercourse from cross-reaction with human prostatic antigen), allergen immunotherapy-AIT (likely ineffective in patients with exclusive sensitization), and preventive measures (possibility to own a female dog and a likely reduction of allergen passive transport) (**figure 2**) (11-16). The results of this study emphasize the need of an adequate management of patients suffering from dog allergy, especially those with significant clinical symptoms following dog exposure. A detailed collection of anamnestic data (including modalities of exposure to dogs and sex of dogs with more frequent contact), clinical and routine diagnostic examinations integrated by CRD may represent the base for a correct management of these patients. In this scenario, the microarray technique for available animal allergens could be useful to evaluate the possibility of cross-reactions between allergens of different animals and in the management of Can f 5 positive patients, as reported in **figure 2** (17,18). In conclusions, although our data are limited to North East Italy, they confirm that the frequency of Can f 5 as sensitizing dog allergen is high, as demonstrated by the number of sensi-

tized patients and the level of allergic sensitization. These results should be taken into account by allergists managing dog allergic patients. Further studies are needed to better explore the multiple aspects (with clinical implications) related to Can f 5 sensitization as previously described. Finally, we are also planning further studies to establish the prevalence of allergic sensitization to Can f 5 in Italy.

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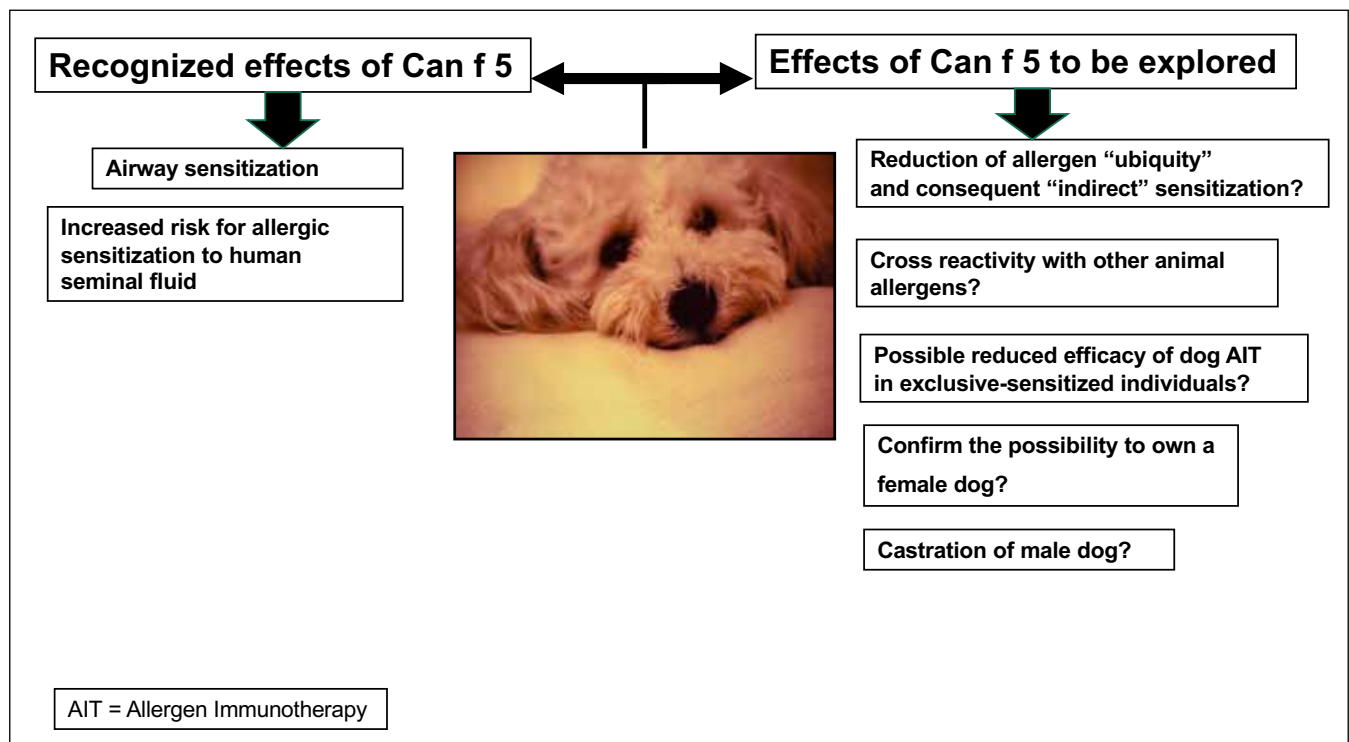
### Conflict of interest

All authors declare that they have no conflict of interest.

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**Figure 2** - Possible topics associated with a prevalent or exclusive allergic sensitization to Can f 5. Adapted from (10). (The picture of the dog "Charlie" 2001 - 2017 is property of GL).



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