

CORRESPONDENCE

Clinical relevance of sensitization to cross-reactive lipocalin Can f 6

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We read with great interest the article by Nilsson et al. (1) on the new dog allergen Can f 6 – a lipocalin that displays 67% amino acid identity with Fel d 4 and 55% with Equ c 1. IgE reactivities to Can f 6, Fel d 4 and Equ c 1 in 100 dog sensitized individuals suggested cross-reactivity of the three lipocalins. Two patients with a doctor's diagnosis of cat, dog and horse dander allergy were selected for basophil activation tests that demonstrated a patient-dependent activation pattern with either Can f 6 or Equ c 1 as the most potent activator – possibly reflecting differences in primary sensitization. Sera with IgE reactivity to all three allergens were selected for ELISA cross-inhibition experiments that showed variable degrees of cross-reactivity between the subjects. Data from two representative patients are displayed, one of them shows an almost complete inhibition of IgE binding to Can f 6 by Equ c 1 and only a negligible inhibition of IgE binding to Equ c 1 by Can f 6. The authors conclude that Can f 6 is a likely candidate for cross-species sensitization with cat and horse and that different pattern of cross-reactivity may point to the primary sensitizing source and can provide important information prior to specific immunotherapy.

Unfortunately, little or no clinical data on the patients included in the cross-inhibition experiments were provided, which would allow an assessment of the clinical relevance of the observed cross-reactivities. To add evidence of the clinical importance of this group of cross-reacting lipocalins, we here report the clinical and biological data of three patients allergic to horse and dog. Patient 1 is a 24-year-old patient with a 14-year history of rhinitis and asthma when exposed to horses, and a 2 years history of rhinitis when exposed to dogs. Serology showed elevated sIgE to horse, medium to dog and weak to cat dander. sIgE to available single dog allergens (Table 1) were below 0.35 kU_A/l, with the exception of IgE to Can f 6 which was clearly positive. Reactivity to Can f 6 could be totally inhibited with Equ c 1, strongly suggesting that horse was the primary sensitizer and that not only the positive test to dog but also the clinical symptoms to dog were due to cross-reactivity with Equ c 1.

Patient 2 was first seen at the age of 8 for acute rhinitis, conjunctivitis and asthma in the presence of horses. From the age of 14 onwards, the patient developed perennial asthma at a time when there was no contact with horses but while the family acquired dog. Specific IgE checked at the age of 18 were strongly positive to horse (Table 1), medium for dog and low for cat. Specific IgE to dog allergen components were at 4.2 kU_A/l for Can f 1, negative for Can f 2

Table 1 Serological data of horse and dog allergic patients

	Patient 1	Patient 2	Patient 3
Horse dander (kU _A /l)	92	>100	>100
Dog dander (kU _A /l)	7.2	30	>100
Cat dander (kU _A /l)	0.72	7.64	>100
rEqu c 1 (kU _A /l)	18	52.4	>100
rCan f 1 (kU _A /l)	<0.1	4.42	25.0
rCan f 2 (kU _A /l)	<0.1	0.26	5.3
nCan f 3 (kU _A /l)	0.17	<0.1	14.6
rCan f 5 (kU _A /l)	<0.1	0.5	<0.1
rCan f 6 * (kU _A /l)	3.7	14.0	55.7
Max. inhibition (%) of Can f 6 by 100 µg/ml Equ c 1	90%	90%	89%
>80% inhibition of Can f 6 by (x) of Equ c 1	(1 µg/ml)	(1 µg/ml)	(0.1 µg/ml)
Max. inhibition (%) of Equ c 1 by 100 µg/ml Can f 6	32%	63%	62%

IgE values were determined by ImmunoCAP (ThermoFisher Scientific, Uppsala, Sweden), excepted of those marked by *, which were quantified by ELISA. Inhibitions were carried out by ELISA.

and Can f 3, weakly positive for Can f 5, but 14 kU_A/l for Can f 6. IgE reactivity to Can f 6 was reduced to baseline by inhibition with Equ c 1 (at 1 µg/ml). This suggests that IgE to horse Equ c 1 could have at least partly been responsible for the clinical symptoms upon dog exposure due to cross-reactivity with Can f 6.

Patient 3 was seen at the age of 19 because of rhinitis and asthma attacks while being with his girlfriend who owned a dog. At the age of 5, he had experienced asthmatic problems when in contact with horses, cats or dogs. Specific IgE now performed were strongly positive to horse (Table 1), cat and dog. Specific IgE to Can f 6 were at 55 kU_A/l and could be completely inhibited with Equ c 1. However, specific IgE were also positive for the other dog allergens, including dog serum albumin, making it very unlikely that that cross-reactivity with Equ c 1 alone played an important role in the clinical symptoms provoked by exposure to dogs.

In conclusion, we would like to emphasize that IgE cross-reactions within the newly described lipocalin family (1–3) are not only important in patient diagnosis but that they have also clinical implications.

Conflict of interest

TJ has received research grants, honoraria and consulting fees from Phadia, Germany, now Thermo Fisher Scientific, Germany. CH and FH have no conflict of interest to declare.

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