Karolinska Institutet

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New approaches for diagnostics and therapy of allergy to pets

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ABSTRACT

Allergic diseases have been described already in 900 AD but today allergic diseases have reached epidemic proportions. About 30% of the world population is affected. Typical allergic symptoms of the immune system's reaction to allergens are runny nose, red eyes or skin reactions like itching, eczema, urticaria, as well as more severe symptoms like asthma and anaphylactic reactions. The overall aim of this thesis was to identify and characterize new pet allergens and to use these to improve diagnostics and prediction of pet allergy. Furthermore, to provide a relevant platform, a mouse model reflecting chronic asthma, for the development of novel treatment strategies for cat allergy.

In the first paper we studied dog saliva as a source of new allergen molecules for improved diagnostics of allergy to dog. We show that there are at least 12 protein bands in dog saliva that are recognized by IgE antibodies from dog-allergic patients. Several of those bands were not identified in dog dander extract. Furthermore, we demonstrate that about one-fifth of patients with symptoms to dog, but lacking IgE antibodies to dog dander, were IgE positive to saliva. Dog saliva was shown to be a significant allergen source that should be taken into account for improved diagnostics of dog allergy. Combining dog dander and dog saliva or spiking dog dander extract with dog saliva would be beneficial for developing enhanced dog allergy diagnostics.

In the second paper of this thesis we investigated the prevalence of sensitization to the novel cat allergen Fel d 7 in 94 cat-sensitized patients and elucidated Fel d 7's allergenicity and cross-reactivity with the homolog major dog lipocalin allergen Can f 1 on an epitope level. More than a third of the Swedish cat dander-sensitized patients, 39%, were IgE positive to Fel d 7 and we could show that Fel d 7 is a biologically active allergen. Our results demonstrate that Fel d is cross-reactive with Can f 1 and indicate that Fel d 7 has epitopes in common with Can f 1 which contributes to the co-sensitization observed in patients with allergy to cat and dog. Also, Can f 1 peptides spanning the Can f 1 sequence were used to map Fel d 7 binding epitopes in a 3D model based on the known structure of a human lipocalin homolog.

Paper III describes the association between sensitization patterns to individual cat and dog allergen molecules during childhood and symptoms to these furry animals up to 16 years of age. We investigated sensitization to individual cat and dog allergen molecules in childhood through adolescence using the BAMSE (Barn/Children Allergy/Asthma Milieu Stockholm Epidemiologic study) birth cohort. Sera and questionnaire data from 779 randomly collected children at 4, 8 and 16 years were examined. IgE reactivity to cat and dog allergen molecules were analyzed with the MeDALL (Mechanisms for the Development of ALLergy) chip. This is the first study to elucidate the usefulness of analyzing the individual cat and dog allergen molecules as predictors of cat and dog allergy development from childhood to adolescence. We report that IgE to Fel d 1 is as good as IgE to cat extract for diagnosis of cat allergy and IgE to Can f 1 is superior to IgE to dog allergen extract for diagnosis of dog allergy. Thus, molecular-based allergy diagnostics may offer new opportunities for improving diagnosis of pet allergy and in particular allergy to dog.

The last paper presents a relevant model for cat allergen-induced asthma in mice, exhibiting features of human chronic disease. Female BALB/c mice were presensitized with rFel d 1 adsorbed to Alum and subsequently challenged intranasally (i.n.) with cat dander extract (CDE) three consecutive days per week during five weeks. The new animal model displays hallmarks of chronic allergic asthma mimicking human disease, e.g. airway hyperresponsiveness, a mixed neutrophilic and eosinophilic inflammatory response in the lung, proinflammatory cytokines and remodeling in lung tissue. This paper provides a relevant model for studying chronic allergic disease induced by a natural airway allergen. Thus, the model is suitable for testing novel strategies for cat allergy vaccination, for evaluating and developing new treatments of human disease.

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