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Key Words

Profilin
Pan-allergen
IgE
Cross-reactivity
Plants

Profilin, a Novel Plant Pan-Allergen

Abstract

Recently we identified birch profilin as a novel pollen allergen which showed significant sequence homology with profilins from different eukaryotic organisms. Profilins were described to control actin polymerization and to participate in signal transduction via the phosphoinositide pathway, but have so far been unknown in plants. The ubiquitous occurrence of profilins in eukaryotes led us to the hypothesis that profilins may fulfill similar functions in plants as known in other eukaryotes. Here we report on the identification of profilins as functional plant pan-allergens in distantly related plants. The ubiquitous occurrence of profilins in distantly related plants as allergenic structures provides a molecular basis for the frequently observed phenomenon of cross-sensitization towards distantly related plant species in allergic patients.

Introduction

Allergic reactions towards different plants and plant products (pollen, plant-derived food) are frequently observed. Such cross-reactivities were described between tree pollen allergens, apples, and nuts [1-3] as well as between mugwort and celery [4]. The presence of common allergenic structures in all these different plant species would provide an explanation for this phenomenon. The major birch pollen allergen *Bet v* I which was found to be highly homologous to pathogenesis-related plant proteins [5] is a good example for a cross-sensitizing structure between the related trees of the fagales order (birch, alder, hazel, hornbeam and oak) [6] and plant-derived food stuff [2]. The wide distribution of this allergen may be due to its biological function as a plant-defense protein. Recently we identified profilin as a novel birch pollen allergen and described in profilin-allergic patients a first example of an IgE autoreactivity against human profilin

[7]. Although birch and human profilin share only a low sequence identity, this homology was sufficient to account for a weak cross-reactivity of patients' IgE and may be responsible for the maintenance of a constantly high anti-profilin IgE titer in profilin-allergic patients outside the pollen season. The further identification of the profilins as a novel class of functional plant pan-allergens provided the molecular basis for allergic cross-sensitizations to distantly related plant species [8, 9]. This paper is thought to briefly sum up our knowledge of profilins as plant pan-allergens.

Occurrence and Properties of Plant Profilins

Profilins were originally described in different eukaryotic organisms but have been unknown in plants. Using poly(L-proline)-Sepharose [10], we purified profilins from pollens of far distantly related plant species (trees,

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1018-2438/92/0994-0271
\$2.75/0

grasses and weeds) and coined the term plant pan-allergens for the profilins [8]. We further showed that pollens of distantly related plants such as monocotyledons and dicotyledons, angiosperms and gymnosperms contain large amounts of profilin and demonstrated that profilins represent a novel class of actin-binding proteins in plants [11]. The dissociation of the pollen profilactin complex may be one of the key mechanisms involved in pollen germination and pollen tube growth, comparable to the acrosomal reaction of echinoderm sperm [12, 13]. However, profilins also seem to be constitutively expressed in somatic tissues of plants where different isoforms can be found [14]. This provides a good explanation for the presence of profilins as allergenic components in vegetables and fruits [2, 3, 15]. The ubiquitous distribution and conserved biological functions of plant profilins may therefore be responsible for the importance of these proteins as plant pan-allergens.

Structural Similarities of Different Plant Profilins

So far cDNA sequences are available from two different plant profilins which were derived from a dicotyledonic plant, birch (*Betula verrucosa*) [7] and a monocotyledonic plant, timothy grass (*Phleum pratense*) [11, 16]. Despite the distant botanical relationship of these plants, both sequences are 80% identical. In addition, we showed that rabbit antibodies which were raised against purified celery profilin [15] and purified recombinant birch profilin [11] cross-react with almost all plant profilins. These data indicate the close structural relationship of plant profilins and provide an explanation for the similar capacity of these proteins to bind allergic patients' IgE. About 20% of all pollen-allergic individuals show IgE reactivity to profilin which, therefore, represents an important allergen although it is not a major allergen in a single plant species.

Specific Potential of Profilins to Release Histamine from Allergic Patients' Basophils

Allergens have to be tested for their specific IgE-binding properties as well as for their functional properties in cellular systems. In addition to the IgE-binding capacity of profilins from different plant species (trees, grasses and weeds) and recombinant birch profilin [8], we compared the properties of all these profilins to release histamine from basophils of profilin-allergic individuals [8, 17]. All purified plant profilins as well as the purified recombinant

birch profilin showed comparable IgE-binding capacity and ability to release histamine from the patients' basophils via membrane-bound specific IgE.

Model Allergen Concept

The structural similarity of the plant profilins already indicates a similar potential to bind IgE antibodies. We tested profilins from far distantly related plants (trees, grasses and weeds) [8], profilins from different plant tissues (pollen and fruits) [3, 14, 15] as well as recombinant birch profilin for the presence of common IgE epitopes. IgE antibodies of all patients cross-reacted with the different profilins, and binding of IgE to the different profilins could be blocked by preincubation of the sera with purified recombinant birch profilin expressed in *Escherichia coli* [8]. This indicates that allergen-specific diagnosis and therapy possibly requires only a few, probable recombinant, model allergens instead of a mixture of almost identical molecules from different species. This concept should apply for the plant profilin family [8], the major pollen allergens of trees belonging to the fagales order (birch, alder, hazel, hornbeam, oak) [1, 6] and for grass pollen allergy, where we could show that allergy can be sufficiently diagnosed with three to four recombinant grass pollen allergens from one species (timothy grass, *Phleum pratense*) [16].

Conclusion

The discovery of profilin as a birch pollen allergen [7] provided us with a novel type of allergen, which is widely distributed in different plant species. Pollen profilins from different plant species (trees, birch; grasses, timothy grass, and weeds, mugwort, ragweed [19] and profilins from different plant tissues (fruits, leaves and roots) share IgE epitopes and release histamine from blood basophils of allergic patients. Profilins represent therefore important cross-sensitizing allergens in pollens and plant-derived food which led to their designation as plant pan-allergens. The finding that due to cross-reactivities only a small number of relevant allergens can be defined led to the concept of using a few model allergens for diagnosis and possibly therapy of pollen and food allergy.

Acknowledgements

This work was supported by grant 3/8603 of the 'Fonds zur Förderung der gewerblichen Wirtschaft' and by grant S6002 Bio of the 'Fonds zur Förderung der wissenschaftlichen Forschung'.

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