

**Mini
Review**

Plant Allergic Proteins and Their Biological Functions

LI Dong-Dong, [HE Shao-Heng](#)*(*Institute of Allergy and Inflammation, Medical Collage of Shantou University, Shantou 515031, China*)

Abstract Pollen, fruit and latex in plants can induce allergic diseases like rhinitis, asthma and hay fever. These are classified into inhalent allergens, ingestent allergens and contactant allergens. Recent research showed that these plant allergens are responsible for specific and vital biological function for plants too. Studies on those allergenic proteins will be beneficial for immunotherapy and botanic research. Currently, research on the plant allergens and their related allergic diseases is setting up a novel and cross-subjects field involving plant molecular biology, immunology and allergy.

Key words plant; allergic proteins; function; allergy

Type I hyperresponsiveness that affects almost 25% of the population in industrialized countries and more than 130 million people worldwide[1, 2], represents a complicated immunodisorder related to formation and actions of immunoglobulin E (IgE). Immediate type symptoms of allergic rhinitis and asthma result from the cross-linking of effector cell-bound IgE by allergens and the subsequent release of biological mediators (e.g., histamine, leukotrienes) from these cells. As one of the most widespread allergic substances, the allergens in plants are hard to avoid and have obvious regional and seasonal traits. Now, identification and characterization of these plant allergens is considered as one of the keys for the diagnosis and treatment of allergic diseases.

1 Classification of allergens in plants

1.1 Inhalent allergens

Inhalent allergens from grass or tree pollens, house dust mite and animal dander are the major substances that are capable of provoking type I hyperresponsiveness. Among those allergens, one of the most common ones is pollen of plants[3]. An individual who has hypersensitivity to pollen often suffers from seasonal allergic rhinitis or extrinsic asthma. Weeds, grasses and trees are common sources of pollen, and high concentrations of these pollen allergens in the air surrounding us correspond well to pollen-related hypersensitivity disease. The major and most widespread allergenic components of pollen is the group I allergens. Thus, the allergy caused by these allergens is often termed "seasonal". These allergenic proteins in pollens with molecular weight about 30 kD are quickly and profusely released by grass pollen upon hydration[4]. In recent years, research in this area has focused on the characterization of relevant grass pollen allergens because as many as approximately 40% of allergic individuals start their symptoms immediately after contacting with grass pollens[5].

1.2 Ingestent allergens

Ingestent allergens often refer to substances inducing allergy after the sensitized individuals eating a certain food. Typical symptoms of this type allergy include mouth or throat itching and lip swelling. In recent years, an increase in tree nut and peanut allergy has been reported in Europe and in US. For example, peanut and/or tree nut allergy affect approximately 1.1% of US population, corresponding to 3 million individuals at risk of adverse reaction to these foods[6]. Of these individuals, 50% considered in the survey performed by Sicherer et al.[7] were reactive to peanut, 30% to walnut and 10% to almond, while only 4% were reactive to both peanut and tree nut. In previous reports, the percentage of allergic individuals symptomatically reactive to two or more nuts has been found to be nearly 10%, which corresponds to at least half a million individuals in the world reactive to two related nuts. On the other hand, a recent study reported that approximately 35% patients with pollen allergy were also sensitive to fresh fruits and vegetables[8].

1.3 Contactant allergens

Latex is the most important contactant allergens in plants. Since the late 1980's, this immediate-type allergy provoked by natural rubber products has been reported around the world[9]. It is now known as latex allergy. It also can be induced by wide-ranging latex products. In addition, allergy to exotic fruit is frequently reported in studies on latex-allergic subjects. Subjects suffering from the latex-fruit syndrome become primarily sensitized to latex and then develop food allergy as a result of cross-reacting IgE against protein, such as in banana and avocado[10]. Nowadays, plant defense-related proteins induced by stress were reported as a main kind of latex allergen.

2 The biological functions of allergens in plants

In last decade, with the implementation of molecular biological techniques in the field of allergen characterization, the sequence, nature, and three-dimensional structure of several important allergens have been revealed. Application of molecular cloning techniques also enable us to understand the natural functions of the IgE-binding proteins in plants. There are at least three major biological functions for the allergens in plants.

2.1 Calcium-binding protein

In plant molecular biology, calcium in pollen is recognized as an essential constituent of in vitro pollen-germination media and a potential chemoattractant guiding pollen growth. In 1999, Rozwadowski et al.[11] characterized calcium-binding protein from Brassica and Arabidopsis pollen. By sequence comparison, the protein was revealed as a part of a family of pollen allergens identified recently in several evolutionarily distant dicot and monocot plants. The protein also has strong immunoreactivity to IgE from a human subject allergic to Brassica pollen[12]. In addition, the members in the two EF-hand allergen families share an average sequence identity of 77%, which is of comparable magnitude within and outside the calcium-binding domain. In fact, several kinds of plant allergens with EF-hand calcium-binding domains have been identified in birch[13], Bermuda grass[14] and rapeseed[12]. Calcium binding plant proteins have now been discovered as relevant cross-reactive allergens, and the EF-hand domain is the major epitope for antibody reorganization in those allergens[15].

2.2 Pathogenesis-related protein (PR protein)

PR proteins which represent an important group of human allergens can be up-regulated in plants in response to stressors such as freezing, drought, temperature, fungi, viruses or bacteria infection. So far, several allergenic PR proteins have been biochemically characterized. They belong to different PR protein groups (there are 10 groups of PR proteins in nature). For example, Jun a 3, the allergen in mountain cedar, was found to be homologous to the PR-5 protein group. Plant allergens Bet v 1 (in birch), Mal d1 (in apple) and Dau c 1 (in carrot) are members of PR protein 10 group[16]. Similarly, the major allergen in rubber Hev b6[17] and its metabolic products, Bar r 2 (in turnip)[18] and Pers a 1 (in avocado)[19] have the properties of chitinase, and belong to the PR protein 4 group. Investigation of potential common functions and structures of PR-proteins will uncover some "law" of allergens in plants and will explain the reason for cross-reaction phenomena in plant allergens.

2.3 Expansins

A cell wall-loosening agent, is extracellular protein that promotes plant cell wall enlargement by disrupting

noncovalent bonding between cellulose microfibrils and matrix polymers[20]. When the first expansin complementary DNA was sequenced, BLAST searches in GenBank revealed a distant sequence similarity to a group of grass allergens called group-1 allergen. It was characterized further that group-1 allergens in plants were indeed structurally and functionally related to expansin, and that their vegetative homologs comprise a second family of expansins, such as Lol p I (in ryegrass), Ory s I (in rice) and Zea m I (in maize)[4]. But different from the original group of expansin, this group of expansin in pollens could only induce extension in the cell walls of grass and was not effective on the walls from dicotyledons[21]. Recently, the cell wall-loosening agents in pollens have been named as 'A'-expansin family, in order to distinguish it from the original group of expansins, which are now called 'A'-expansins. In type I hyperresponsiveness, there are varieties of cross-reaction between allergens in different plants[22]. The common conservative domain and/or isotope among different allergens in plants are the radical cause of these phenomena. Thus, research on identification and characterization of allergens and their structures and biological functions will be benefit for the diagnosis and treatment of pollen related allergic diseases.

3 Progress in gene cloning and recombinant protein production of plant allergens

Allergen-specific immunotherapy (SIT) represents one of the few curative approaches toward type I hyperresponsiveness[23]. But, there are three major problems associated with SIT: first, presently SIT is performed with natural allergen extracts, containing mixtures of allergens, nonallergenic and/or toxic proteins, and other macromolecules, which are hard to standardize. Second, systemic administration of allergen can cause severe IgE-mediated side effects during the treatment on patients, and third, therapeutically effective dose often cannot be achieved because of non-standardized extracts or side effects. With the clarification of the nature, sequence and three-dimensional structure of several important allergens, molecular level recognition of allergens and IgE antibodies will become available. To date, cDNA sequence of 60 pollen allergens from 27 plant species have been deposited in the allergen databank (www.allergen.com). Since pure and standardized recombinant allergens can be formulated to replace natural extracts, using genetic engineered allergens for SIT become a possible and promising method for immunotherapy. In last decade, a variety of recombinant allergens from plants, mites, molds, mammals and insects have been expressed using various systems, such as E.coli[24], Pichia[25] and plants[26]. Moreover, the recombinant allergens can be engineered to reduce the risk of the IgE-mediated side effects. The molecules with reduced allergenicity (hypoallergen) would not lead to anaphylactic reaction upon injection and would allow higher-dose administration of allergen, which has showed to be more effective in symptom reduction than low dose. In this way, high dose of allergen can be administered to allergic patients, which increases the efficacy of the treatment. Based on this consideration, site-directed mutant and conformation has been applied in the recombination of hypoallergens[27, 28]. The clinical use of these products may lead to not only improve diagnostic specificity and sensitivity but also safer and more effective immunotherapy.

4 Summary

As the most widespread species on the earth, plant is a part of the human normal life. It is hard to avoid plant allergens from trees, grasses and weeds. Although specific immunotherapy represents a curative approach toward allergy, the mechanism operating in SIT still remains not completely understood. In recent statistics, there has been a significant increase in the prevalence of allergic disease over the past 2 to 3 decades. Currently, more than 130 million people suffer from the asthma and the numbers are increasing [29]. There is a research considering that air pollutants from industry and automobiles are cofactors contributing to recent increase in allergic disease and asthma[30]. On the other hand, man cannot ignore transgenic plants are widespread in the modern world, it could be the source for new kind of allergens.

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*Corresponding author: Tel, 86-754-8900405; Fax, 86-754-8900192; e-mail, shoahenghe@hotmail.com