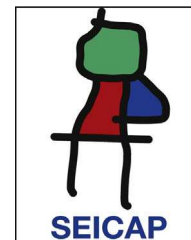


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EDITORIAL

Are profilins relevant allergens or confusion allergens?



Advances in the techniques used to study allergic patients have allowed us to recognize multiple mistakes made in the past, and thus to avoid prescribing patient immunotherapy treatments that are not fully valid.

One of the major achievements has been the molecular diagnosis of allergic diseases. In effect, while in the past we only had gross determinations of specific IgE to pollens, we can now identify which specific protein triggers the allergic reaction in many of our patients. Moreover, a group of these proteins are known to cluster in panallergen families which exhibit great similarity in their three-dimensional structure, causing the emergence of cross-reactions between the proteins. Several panallergen families have been identified – the profilins being an example of great clinical relevance.

Profilins are small proteins with a molecular weight ranging between 12 and 19 kDa, and are present in all eukaryotic organisms,¹ including plants.² They participate in numerous biological processes such as cell cytoskeletal reorganization and the regulation of actin polymerization–depolymerization. They likewise intervene in cell structure and mobility, and play a critical role in cell division, embryogenesis and cytokinesis.

Unlike plant calcium binding allergens from plants, which are present in most pollens, profilins are part of the storage tissues of plants (fruits, nuts, spices, latex) and, therefore, are also responsible for cross-reactivity between pollens and foods, and even between pollens and latex. Of all cases of cross-reactivity in pollen-food syndrome, profilin sensitization accounts for at least 20%.³

Profilins have highly preserved sequences, with identities of between 70 and 85% (Ole Bet v2 and Ole e2) and a prevalence of 20% in most patients allergic to pollen. However, there are exceptions such as *Chenopodium* profilin (*Chenopodium album*, Che 2), with a reported prevalence of 50% that has caused it to be regarded as the major allergen.^{4,5}

Profilin was first described more than three decades ago, with a molecular weight of 15 kDa, joined the monomers and inhibited actin polymerization; as a result, these proteins are named after their property of maintaining profilamentous actin (PRO-FILamentous actIN).

Profilins as allergens are found in pollens of *Phleum pratense* (Phl p 12), *Cynodon dactylon* (Cyn d 2), *Artemisia vulgaris* (Art v 4), *Zea mays*, *Triticum aestivum*, *Parietaria judaica* (Par j 3), *Chenopodium album* (Che a 2), ambrosia elatior, *Olea europaea* (Ole e 2), *Corylus avellana* (2 Cor), *Agnus agglutinosa*, *Castanea sativa*, palm (Pho d 2), *Mercuriales annua* (Mer 1), and also in plant foods such as apple (Mal d 4), peach (Pru p 4), melon (Cuc m 2), watermelon, banana (Mus xp 1), celery (Api g 4), carrot (Dau c 4), hazelnut (Cor a 2), peanut (Ara h 5), cherry (Prop av 4), pear (Pyr c 4), pineapple (Ana c 1), tomato (Lyc e 1), soybean (Gly m 3), pepper (Cap 2) and even latex (Hev b 8).^{5,6}

With respect to tree pollens, there is cross-reactivity in families of the order Fagales, including birch, hazel, alder, hornbeam and beech, with their respective allergens Bet v 1, Cor a 1, Aln g 1 and Car b1, for which there is a sequence identity of over 70%. Oleacea is of particular relevance, since Ole e 1 has high sequence identity with homologous allergens: 91% with Fra e1, and 88% and 90% with Lig v1 and v1 Syr.^{4–7}

Allergenic plant profilins are highly preserved amino acids sequences. In contrast, non-allergenic profilins from other eukaryotes have lesser identities of close to 30%. One aspect worth noting is that the sequence of the amino and carboxyl terminals of profilins in lower animals, plants and fungi are highly preserved, whereas among vertebrates they are highly divergent. This feature is responsible for the cross-reactivity that occurs in this family of panallergens.⁸

In northern and central Europe profilins have been identified as one of the four major allergens, because patients allergic to Rosaceae cross-react with birch pollen and/or grasses, with the recognition of specific IgE for profilin in less than 20% of the patients.⁹ In Spain sensitization to date palm, a common tree in the Mediterranean region, ranges from 5.6% in Elche to 29.4% in Zaragoza, but this type of pollen has not been found in monosensitized patients – thus suggesting cross-reactivity between pollens.¹⁰ Indeed, palm pollen extracts contain between 25 and 50 times the amount of the grass profilin.¹¹

It is at this point that mention should be made of the article reviewing “Profilin sensitization in a Mediterranean

population''. This study aimed to describe the increased prevalence of sensitization to profilin through prick test techniques using date palm pollen (Pho d 2) in patients with respiratory disease living in southeast Spain, identify the profilin profile, and calculate the correlation between sensitization to inhaled profilin and plant allergens with respect to sensitization to plant-derived food allergens. To this effect a large study population of 654 people with an age ranging from 3 to 82 years (mean 24.4 years) was recruited.

This dispersion in the age of the patients is one of the first discordant points of the study, because we have no figures by age groups. In this sense, attempts to assess the pediatric population would be highly influenced by the adult population, in which palm pollen sensitization would be greater if only because of the exposure time.

The aforementioned study used a large battery of allergens in the prick-test, which represent most pollens of the geographical area, including palm tree profiling, as most similar studies already published.^{1,6,10,11} It found no statistically significant association between olive pollen and profilin, or between Cupressus and profilin, though an association was indeed observed with the rest of pollens. This is in contrast to other authors who have evaluated and observed associations, especially with olive.¹²⁻¹⁴

It also should be mentioned that the most common foods implicated in allergic reactions are peach and nuts, and a number of studies support this association.¹³

Although it is true that this is the first study of its kind that takes place in the authors' geographical area, it is not the first published: in 2013 the ESPLORA published the results of a multicentre study designed to determine the profiles of sensitization in pediatric patients between 2 and 14 years of age, and concluded that pediatric patients living in areas of high exposure to many allergens are polysensitized to panallergens. The implementation of new diagnostic tools is therefore essential for establishing a correct diagnosis.¹⁵

There are even authors who claim that the detection of IgE reactivity to a single protein marker (Bet v 2) would be sufficient to diagnose or rule out sensitization to profilin. The detection of IgE against multiple homologous protein allergens with no cross-reactivity is clinically more informative, although increases the risk of confusion or misinterpretation.¹⁶

In conclusion, although the passing of time has led physicians to adapt to new research techniques, such as molecular diagnostic procedures, we are in danger of forgetting that the allergic patient is not a poly-prick test patient; we should use these techniques to obtain further information and especially to avoid errors in prescribing immunotherapy.

References

1. Jockusch BM, Murk K, Rothkegel M. The profile of profilins. *Physiol Biochem Pharmacol*. 2007;159:131-49.
2. Valenta R, Duchene M, Breitenbach M, et al. A low molecular weight allergen of white birch (*Betula verrucosa*) is highly homologous to human profilin. *Int Arch Allergy Immunol*. 1991;94:368-70.
3. Valenta R, Duchene M, Ebener C, et al. Profilins constitute a novel family of functional plant pan-allergens. *J Exp Med*. 1992;175:377-85.
4. Pomés A, Villalba M. Alérgenos. *Tratado de Alergología*. Madrid: Ed Ergon; 2007.
5. Barderas R, Villalba M, Rodríguez R. Recombinant expression, purification and cross-reactivity of chenopodium profilin r Ch a 2 as a good marker for profilin sensitization. *Biol Chem*. 2004;385:731-7.
6. Valenta R, Duchene M, Pettenburger K, et al. Identification of profiling as a novel pollen allergen; IgE autoreactivity in sensitized individuals. *Science*. 1991;253:557-60.
7. Lombardero M, Obispo T, Calabozo B, et al. Cross reactivity between olive and the other species. Role of Ole e 1 related proteins. *Allergy*. 2002;57:29-34.
8. Radauer C, Breiteneder H. Pollen allergens are restricted to few protein families and show distinct patterns of species distribution. *J Allergy Clin Immunol*. 2006;117:141-7.
9. Landa-Pineda CM, Guidos-Fogelbach G, Marchat-Marchan L, et al. Profilinas: alérgenos con relevancia clínica. *Rev Alerg Mex*. 2013;60:129-43.
10. Huertas JR, Lavin JR, García-Cervantes AM. ¿Es la sensibilización al polen de palmera una expresión de la alergia a las profilinas en el área mediterránea? *Alergol Immunol Clin*. 2005;20:175-80.
11. Ibarrola I, Eraso E, Arilla MC, et al. Profilin: a major allergen in date palm (*Phoenix dactylifera*) pollen allergy. *Allergy*. 2002;57 Suppl. 73:283-4.
12. Asturias JA, Arilla MC, Gómez-Bayon N, et al. Cloning and expression on the panallergen profilin and the major allergen (ole e 1) from olive tree pollen. *J Allergy Clin Immunol*. 1997;100:365-72.
13. Boyano-Martínez T, Pedrosa M, Belver T, et al. Peach allergy in Spanish children: tolerance to the pulp and molecular sensitization profile. *Ped Allergy Immunol*. 2013;24:168-72.
14. Palomares O, Swoboda I, Villalba M, et al. The major allergen of olive pollen Ole e 1 is a diagnostic marker for sensitization to Oleaceae. *Int Arch Allergy Immunol*. 2006;14:110-8.
15. Feliu A, González de Olano D, González E, et al. A multicenter study of sensitization profiles in an allergic pediatric population in an area with high allergen exposure. *J Investig Allergol Clin Immunol*. 2013;23:337-44.

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