

# EVALUATION OF SENSITIZATION TO MAJOR AND MINOR RECOMBINANT ALLERGENS TO BIRCH AND TIMOTHY GRASS POLLENS IN FRANCE

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## BACKGROUND

Birch and timothy grass pollens are the main allergens responsible for pollinosis in France. Pollen extracts are mixtures of molecules containing allergens classified as major and minor allergens. An allergen is considered as a major allergen if the sensitization rate is > 50 % among allergic persons. Birch and timothy grass recombinant allergens obtained by genetic engineering have been used for several years for IgE testing. They are particularly useful when patients show multiple sensitizations to pollens because we can identify, inside a family of allergens, which allergen (major and/or minor) is responsible for the symptoms. There is a relationship between an allergy to birch or timothy grass and a high level of major allergen specific IgE.

Previous studies reported sensitization levels to the different recombinant birch and/or timothy grass allergens to determine the sensitization profile of allergic patients (1,2) but few data about the sensitization levels are available. The aim of this study is to evaluate the frequency of mono and poly-sensitization to recombinant birch and timothy allergens, focusing on patients tested for a complete profile of specific IgE (sIgE).

## METHOD

As our lab performs a huge number of allergy tests for mainly French patients, we extracted from our database over the two last years patient sera tested for sIgE against recombinant Bet v 1, Phl p 1, p 5 (major allergens) and Bet v 2, v 4 and/or Phl p 7, p 12 (minor allergens). Specific IgEs were assayed on UniCAP 1000 (Phadia®). As Bet v 2, Bet v 4 and Phl p 7, Phl p 12 are strongly correlated, we combined their results to interpret them.

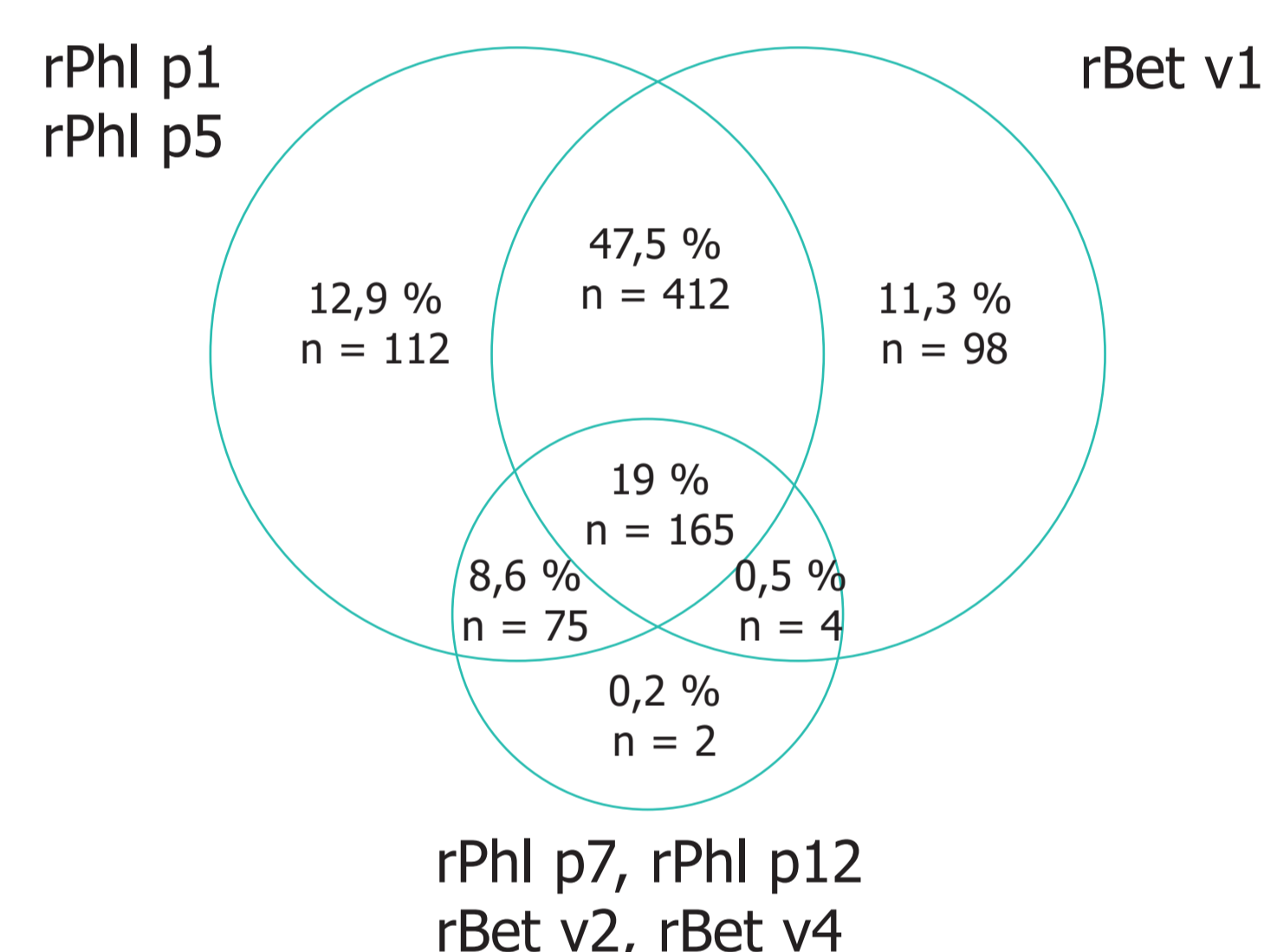
Our study relies on 868 patients between 1 and 82 years old (mean 27), male (46 %) and female (54 %), tested for the whole profile in 2006 and 2007. The detection limit is 0,10 kU/l but we used a positivity cut-off of 0,35 kU/l. With the results we calculated the percentage of positivity corresponding to 3 groups of allergens : Phl p 1+ Phl p 5 (group 1), Bet v 1 (group 2) and the group 3 including the minor allergens (Phl p 7 + Phl p 12, Bet v 2 + Bet v 4).

## RESULTS

Of 868 patients, 112 were monosensitized to Phl p 1, p 5 (12,9 %), 98 to Bet v 1 (11,3 %) and 412 were co-sensitized to both Phl p 1, p 5 and Bet v 1 (47,5 %). Sensitization to Phl p 1, p 5 and Phl p 7, p 12 was found in 75 cases (8,6 %) and sensitization to Bet v 1 and Bet v 2, v 4 was found in 4 cases (0,5 %). Two patients were sensitized to only minor allergens (0,2 %) but 165 patients presented a sensitization to birch and timothy grass major allergens and also to the minor allergens (19 %). So sensitization to major allergens only (Phl p1, p5 and/or Bet v 1) represents 72 % (622 patients for a total of 868) and sensitization to minor allergens is found in 28 % of our patients (244 for a total of 868).

Sensitization to profilin and CaBP concerns 75 patients for a total of 187 patients positive to Phl p 1, p5 (40 %) although it concerns a very limited number of patients in the birch group (4 %).

Frequency of sensitization to recombinant birch and timothy grass allergens in France (868 patients in 2006 and 2007).



## DISCUSSION

Analysing a panel of recombinant allergens, previous studies have reported variable sensitization IgE profiles in European areas. We focused on French patients who had been investigated for specific IgEs against birch and timothy grass pollens recombinant allergens, to obtain sensitization levels to these allergens.

Bet v 1 is the major allergen of birch pollen and corresponds to the PR10 protein (1). It is very specific of allergy to birch pollen but this PR10 is also included in other tree pollens (alder, hazelnut tree) and in fruits and vegetables (apple, cherry, pear, apricot, carrot, celery...). This homology explains the clinical symptoms observed between pollens and food, the oral allergic syndrome or OAS (5).

Phl p 1 is very specific of the allergy to grass.

Bet v 2 and Phl p 12 are minor allergens of birch and timothy grass respectively. They belong to the profilin family (proteins involved in the structure of the pollen cells). They are responsible for numerous cross-reactivities with varied pollens and vegetable food.

Bet v 4 and Phl p 7 are also minor allergens corresponding to a calcium binding protein, allergen found in many plants. This CaBP is a marker of polysensitization to plant pollens (grass, trees, weeds).

We notice that in France, sensitization to timothy grass (12,9 %) is slightly higher than to birch (11,3 %) but sensitization to birch or timothy grass pollens alone is less frequent than co-sensitization to birch + timothy grass (47,5 %). Ghunaim et al (3) who studied patients allergic to grass pollen in Northern Europe (Sweden) noted similar results (19 % of monosensitization to grass but 75 % of patient with grass allergy and a reactivity to Bet v 1. Our results show that many patients belonging to the group "timothy grass" (group 1) react with profilins and CaBP (40 %). This result is very close to what obtained Rossi et al (1) : they found a sensitization rate to the profilin Phl p 12 of 35 % in grass allergic Italian patients. The reason is that these allergens are common in Central and Southern Europe. On the contrary sensitization to profilin seems to be unfrequent in Northern Europe, as shown by Ghunaim (3) who reported that in Sweden very few patients had a reactivity to profilins Phl p 12 and Bet v 2.

Regarding birch, Rossi et al (2) who focused on Italian patients with allergy to birch tested for specific IgE to recombinant birch allergens showed that 58 % were positive to Bet v 1, 45 % to Bet v 2 and 9 % to Bet v 4 but the cross-reactivity with recombinant timothy grass were not studied. In our study we can point out that patients mono-sensitized to Bet v 1 are rarely reactive with profilins : the profilins are found positive for patients sensitized to timothy grass. Specific immunotherapy isn't recommended for patients having such a profile, as birch total extract could induce a sensitization to minor allergens (3).

The recombinant profiles are useful to characterize the reactivity of allergic patients. The results have to be interpreted with the clinical symptoms in order to make a decision as far as immunotherapy is concerned (4). Recombinant allergens are useful as tool for diagnosis of allergy but as reported in recent clinical studies, they also should be useful as immunotherapy product.

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