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Allergens from Olive Pollen Tree and Related Species. Clinical Implications

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Olive tree pollen is important in Mediterranean areas,^{1,2} in contrast with Northern and Central Europe where the pollen from ash tree is an important cause of allergic symptomatology, being the olive uncommon. We started our work having in mind several demonstrated features:

Immunochemical crossreactivity among different Oleacea family members has been described, being specially relevant between olive and ash.³ The epitopic mapping of Ole e 1 (the major antigen from pollen of olive tree) has demonstrated that some antigenic epitopes of this molecule are present in different degree on other

Oleaceae members.^{4,5} The IgE antibody response to Ole e 1 has been associated with DR7-DQ2 antigens.^{6,7}

With these preliminary facts, we asked the following question: **Do all the *Oleaceae* family members share the same genetic restriction pattern in relation to IgE antibody response?** The first step for answering this question, was the study of a population composed by 50 ash allergic individuals, from Switzerland. The sera of these patients, selected by their positive reaction by skin prick test to ash extract, was generously provided by Prof. Brunello Wütrich. These sera were tested for *Olea europaea* and Ole e 1 reactivity in vitro. Forty two patients showed significative levels of IgE antibodies against ash pollen extract and 49 against olive pollen extract. The reactivity to highly purified Ole e 1, was determined by ELISA and DARIA (Double Antibody Radio Immuno

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Assay). The number of patients with IgE anti-Ole e 1 was 42 by ELISA and 35 using the DARIA technique. This difference could be due to technical reasons. Nevertheless, in both cases, the number of patients reactive to Ole e 1 is very high.

These results corroborate the high cross-reactivity between olive and ash pollen. The fact that the major part of allergic patients react to Ole e 1, point to the idea that the main antigen from ash pollen is very close related to the major antigen of olive pollen.

In four individuals sensitized to ash, we typed genomic DNA for **analysis of HLA Class II haplotypes** using reverse dot-blot technique: one was DR7 and three DR3. Although the number of patients studied is very low, these results are in agreement with the genetic restriction pattern described in the IgE antibody response to olive pollen, because DR7 and DR3 are antigens associated in "linkage disequilibrium" with DQ2.

The next step in this study was **the reactivity to different Oleacea family members tested in a population of 40 olive allergic patients from Spain**, previously selected for their Ole e 1 reactivity.

Forty patients sensitized to Ole e 1, were divided in three groups by their haplotypes. All the sera were positive to each extracts, and the higher levels of IgE antibodies were found in the group of DR7-DQ2 individuals, in all the cases. When we compared the reactivity to different Oleaceae pollens with the reactivity to olive pollen, into the group previously established, we found statistically significant differences between Syringa-Olive and Ligustrum-Olive, in the group of DR7-DQ2 patients, and between Olive-Ligustrum, in the DR3-DQ2 patients. However, Olive and Ash did not show any statistically significant difference.

These results, again confirm the high cross-reactivity among different Oleaceae family members, specially between olive and ash, and point to the idea that the response to these pollens could be associated with the same genetic restriction pattern than olive response.

With the main purpose to clarify this question, we decided to perform **cellular experiments of cross-reactivity**. First, we established a T cell line specific to Ole e 1, derived from a patient allergic to olive pollen and second we studied the proliferative response to

different Oleacea family members. Finally, we analyzed in this in vitro assay the genetic restriction for antigen presentation by inhibition with monoclonal antibodies anti-HLA class II and using histocompatible and histoincompatible Antigen Presenting Cells (APC). As APC+s, lympho-blastoid B cell transformed with EBV were used.

The results showed significant proliferative response to all the extracts when the APCs where autologous APCs (DR3-DQ2) and DR7-DQ2, but when we used a non-related APC (YAR, DR4-DQ8), that was generously provided by Prof. Lamb (U. K.), we did not found any response.

We may conclude that DQ2 is implicated in the recognition of all the Oleaceae family members.

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