

Recombinant allergen-based concepts for diagnosis and therapy of Type I allergy

R. Valenta

Department of Pathophysiology, Vienna General Hospital-AKH, University of Vienna Medical School, Vienna, Austria

Rudolf Valenta
Department of Pathophysiology
Vienna General Hospital-AKH
University of Vienna Medical School
Waehringer Guertel 18–20
A-1090 Vienna
Austria

More than 25% of the population suffer from Type I allergy, a genetically determined hypersensitivity disease. The symptoms of Type I allergy (e.g. allergic rhinoconjunctivitis, asthma, atopic dermatitis) are due to the formation of IgE antibodies against *per se* harmless environmental antigens (i.e. allergens). Both, allergy diagnosis and immunotherapy, are still performed with natural allergen extracts consisting of difficult to define mixtures of allergenic and nonallergenic components. During the last decade several research groups have started to characterize the disease-eliciting allergens at the molecular level using molecular cloning techniques and to produce and evaluate recombinant allergens for diagnostic and therapeutic purposes (1) (Fig. 1). Recombinant allergen molecules are not only useful tools to study the immunopathology of the allergic

immune response but will likely advance the diagnosis of IgE-mediated allergies. While diagnosis with the currently applied natural allergen extracts only allows to identify sensitivity of a patient towards certain allergen sources, recombinant allergen-based diagnosis will precisely determine the disease-eliciting allergens and thus the individual patients sensitization profiles (Fig. 1).

Another exciting perspective resulting from the application of recombinant allergens is the possibility to produce recombinant and synthetic allergen-derivatives with strongly reduced allergenic potential for therapeutic purposes (Fig. 1). Such hypoallergenic derivatives will not only allow the treatment of patients according to their individual sensitization profiles but also may contribute to the reduction of anaphylactic side-effects which may occur in the course of allergen-specific immunotherapy (2,3).

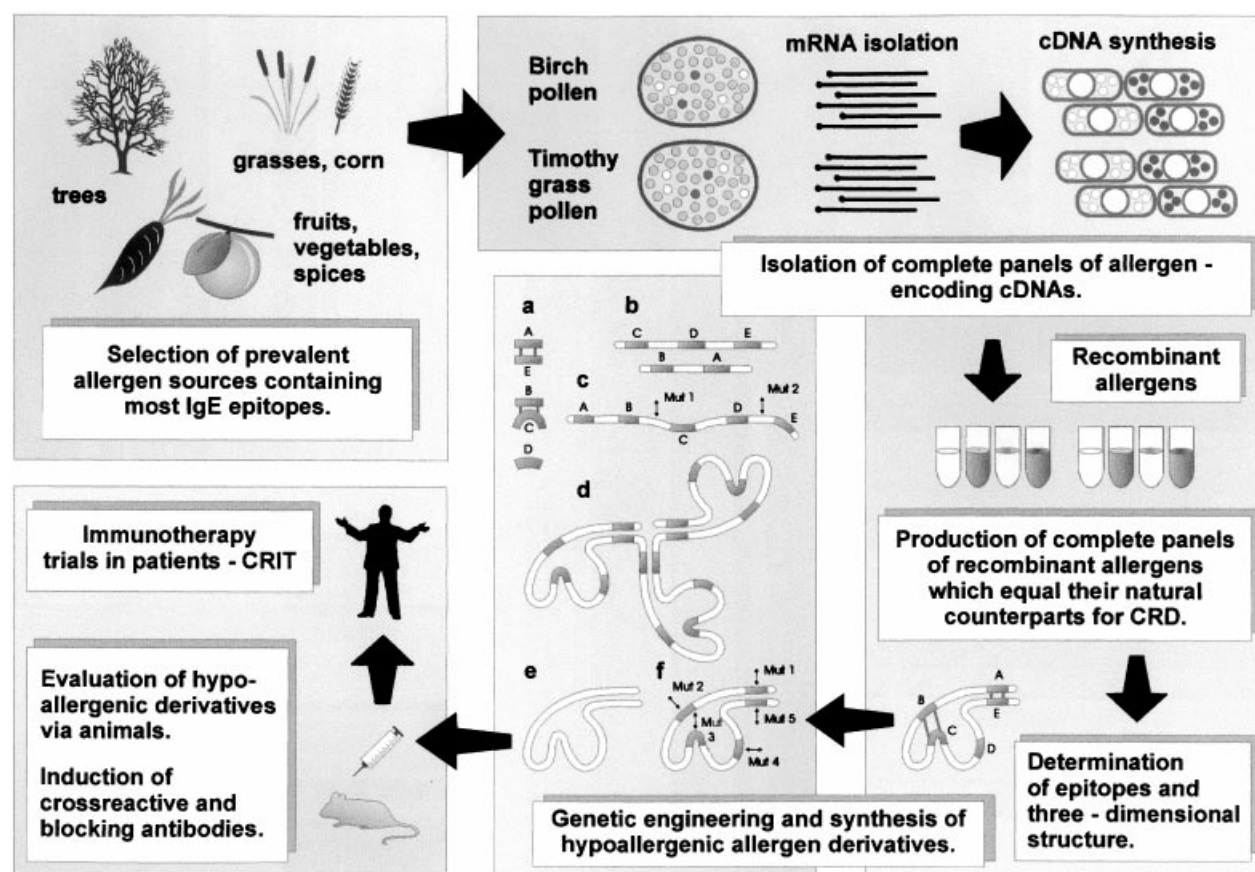


Figure 1. From natural allergen extracts to recombinant allergens for component-resolved diagnosis (CRD) and component-resolved-immunotherapy (CRIT) with hypoallergenic allergen derivatives of IgE-mediated allergies. In the first step relevant allergen sources are selected based on clinical and serological tests. Next, allergen-encoding cDNAs are isolated and the corresponding recombinant allergens are produced. The recombinant allergens are compared with the natural allergens and, if they are equivalent, are then used for component-resolved diagnosis (CRD). They can also be used to study the pathomechanisms of allergy and their immunological and structural properties are analysed. Results of the thorough molecular analysis of the recombinant allergens then allows the development of strategies for the conversion of the active allergens into hypoallergenic allergen derivatives which can be used for component-resolved immunotherapy (CRIT). These strategies are based on the application of recombinant DNA technologies (expression of allergen fragments, oligomers, hybrids and mutants) or the use of synthetic peptide chemistry to produce allergen-derived peptides. The hypoallergenic allergen derivatives must then be tested in experimental animal systems to test whether they can induce protective immune responses and can then be evaluated in clinical immunotherapy trials in patients.

References

1. VALENTA R, LIDHOLM J, NIEDERBERGER V, HAYEK B, KRAFT D, GRÖNLUND H. The recombinant allergen-based concept of component-resolved diagnostics and immunotherapy (CRD and CRIT). *Clin Exp Allergy* 1999; **29**: 896–904.
2. VALENTA R, VRTALA S, FOCKE-TEJTL M, et al. Genetically engineered and synthetic allergen derivatives: Candidates for vaccination against Type I allergy. *Biol Chem* 1999; **380**: 815–824.
3. VALENTA R, KRAFT D. Recombinant allergens. In: HANSEL TT, BARNES PJ, editors. *New Drugs for Asthma, Allergy and COPD*. Basel: Karger, 2001; 195–200.