Recombinant Allergens and Applications

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Abstract: Recombinant DNA technology has great potential in various aspects of allergen-related research and clinical applications. Sufficient amounts of purified wild-type or immunologically modified allergens or fragments have been produced in heterologous expression systems for use in many research fields, such as molecular characterization of the allergen (e.g., three-dimensional structure and epitope mapping), allergen standardization, component-resolved diagnosis (CRD) and patient-tailored specific immunotherapy (SIT). Strategies for obtaining recombinant allergens generally involve three steps, with the choice of heterologous expression system, bacteria, yeast, insect or plant cell, and the purification methods being of major importance. Here we review the major methods used for determining the three-dimensional structure and for epitope mapping, the recent progress in the application of recombinant allergens in clinical research of allergenic disease, such as the recombinant allergen-based microarray diagnosis and therapeutic vaccine.

8.1 Introduction

The first allergen-encoding cDNA was isolated and sequenced a quarter of a century ago (Fang et al., 1988). Since then, the application of recombinant DNA technology to produce sufficient amounts of wild-type or immunologically modified allergens has been a major factor in promoting allergen-related research and clinical practice. Several historical events in research on recombinant
allergens illustrate this progress. The first use of recombinant allergens for in vitro IgE-based diagnosis of allergies was in 1991 (Valenta et al., 1991), and for T-cell epitope studies in 1992 (Yssel et al., 1992). Then the first recombinant hypoallergens with reduced allergenicity were produced (Breiteneder et al., 1993), followed by recombinant allergen use for in vivo skin testing (Moser et al., 1994). In 1996, the three-dimensional structure of the first recombinant allergen was resolved, which can be defined as a milestone in the history of allergy studies (Gajhede et al., 1996). In 1999, in vitro studies (Arquint et al., 1999) and allergen-specific immunotherapy (SIT) (Schramm et al., 1999) with recombinant hypoallergenic derivatives began. Since the year 2000, recombinant allergens have become the most commonly used in clinical research, for example the study of the 3D structure of a specific antigen-allergen complex (Mirza et al., 2000), microarray recombinant allergens for allergy diagnosis (Hiller et al., 2002) and recombinant allergen-based vaccination used in high-efficiency SIT (Niederberger et al., 2004; Pauli et al., 2008). In addition, phase III clinical trials using recombinant allergens in SIT were completed (Valenta et al., 2010).

This section summarizes strategies for obtaining recombinant allergens and gives examples of their current applications based on the latest progress made in these fields.

8.2 Advantages of Recombinant Allergens

Historically, crude aqueous allergen extracts were used in serological and provocation tests. These extracts only indicate the allergen source to which a patient is sensitized, while the precise identity of the disease-eliciting molecule(s) remains unknown. Other major limitations of using allergen extracts for diagnosis include contamination from other sources, differential degradation of the allergen by proteolytic enzymes during extraction and low accuracy of the test due to undefined allergenic and non-allergenic components (Bhalla and Singh, 2008). In comparison, recombinant allergens have many advantages, which can be summarized as follows:

1. They are pure molecules with defined physicochemical and immunological properties which can improve the sensitivity of allergy diagnosis (Crameri and Fluckiger, 2005);

2. The recombinant wild-type allergens can increase our knowledge of the molecular, immunologic, and biological characteristics of allergens;

3. Variants with advantageous properties such as reduced allergenic activity or increased immunogenicity can be used to improve the efficiency of allergy therapy and patient safety;

4. They can be produced as hybrid molecules with the epitopes of several different allergens which can also improve the efficiency of allergy diagnosis and immunotherapy (Valenta and Niederberger, 2007).