

The impact of molecular biology on allergen immunotherapy

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Allergen identification and characterization

The initial impact of molecular biology on allergen immunotherapy had its origins in 1988 when Thomas *et al.* [1] reported the cloning and expression of DNA encoding for the major house dust mite allergen *Der p 1* in *Escherichia coli*. Since then, a large number of allergens have been molecularly cloned and their protein structures identified [2,3]. Not only are proteins known to be allergens, but more recent evidence suggests that carbohydrate moieties may also act as allergens as well [4]. Thus, molecular biology has significantly contributed to our understanding of the allergens involved in allergic sensitization.

Recombinant allergens for the diagnosis of allergen sensitization

The identification of the major allergens from a variety of sources is now being widely used for detection of specific IgE antibodies using techniques such as microarrays [5]. Utilizing component resolved techniques up to 5000 allergens can be tested for IgE binding in a single test. Recombinant DNA technology has also led to epitope mapping studies and the role of T-regulatory cells which are relevant in better understanding allergic mechanisms and potential methods for the treatment of allergic disease (O’Hehir, pp. 559–566). Use of these techniques has led to more comprehensive ways of diagnosing allergic responses and has led to insights regarding the epidemiology of allergic diseases [6].

The use of recombinant technology has also been applied not only to in-vitro assays, but recombinant allergens have also been used for skin testing as well [7]. Further, the molecular composition and biological activity of crude allergen extracts can also be evaluated using recombinant allergen-based immunoassays [8]. Thus, molecular biology has an ever increasing role in the diagnosis of allergic diseases.

Development of immunotherapeutic approaches utilizing molecular biology

A number of microbiological approaches have been utilized as potential approaches for the treatment of

allergic disease. DNA immunostimulatory sequences (ISS) were among the first to be studied [9]. Hypoallergenic allergens have been described based on DNA-based modification of allergens [10]. New developments, including immunization with mRNA-based vaccines, are also under intense investigation (Ferreira, pp. 567–574). In addition, peptide immunotherapy has been a subject of interest as well [11]. A variety of other techniques that are undergoing intensive study include genetically engineered chimeric human Fc-gamma-allergen proteins [12]. Other areas of investigation, such as nanoparticles [13], viral particles [14], and carbohydrate particles [15], may enhance targeting to dendritic cells. These have been used both for conventional subcutaneous immunotherapy as well as sublingual immunotherapy [16].

Novel techniques of allergen immunotherapy

Although this editorial focuses on molecular biologic approaches to immunotherapy, a variety of novel methods to deliver allergen immunotherapy are addressed in this issue of the current opinion. Senti and Kundig (pp. 582–586) discuss epicutaneous immunotherapy, and Jones (pp. 587–593) updates us on new approaches for food allergy.

Recombinant allergen immunotherapy

Recombinant allergens are being used in clinical immunotherapy trials, particularly in Europe. At least two double-blind, placebo-controlled trials have appeared in the literature. One used a mixture of five recombinant grass pollen allergens [17] and the other recombinant *Bet v 1* from birch pollen [18]. Both showed promising clinical results. Pauli (pp. 575–581) provides an update on the clinical status of recombinant allergens for immunotherapy.

Conclusion

In summary, although this editorial comment does not address all the approaches based on molecular biology for the treatment of allergic diseases, there is clear evidence that molecular biology has revolutionized our understanding of the allergens and approaches for treating allergic diseases.

In the end, the ultimate goal is to achieve a well tolerated and effective therapy. Vieths (pp. 594–602) in his article

in the current opinion reviews some of these issues and further information regarding the use of recombinant modified allergens from the U.S. perspective can be found in the review by Rabin [19].

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