

Allergen Immunotherapy

Vaccine Modification



Peter Socrates Creticos, MD^{a,b}

KEYWORDS

• Allergic rhinitis • Allergen immunotherapy • Vaccine modification

KEY POINTS

- New modalities of allergen immunotherapy may allow effective immunization with shorter treatment regimens, improved patient compliance, and the potential of safer agents.
- Toll receptors on specific regulatory cells provide a unique pathway to initiate regulatory pathways capable of down-regulating the untoward allergic diathesis.
- Synthetic peptides offers the ability to immunize allergic subjects with a concise 4-injection intradermal regimen. The smaller peptides are less likely to trigger crosslinking of IgE on mast cells, thereby minimizing the risk of allergic reactions and anaphylaxis.

OVERVIEW

Allergic rhinitis (AR) is a common clinical condition; both its incidence and prevalence seem to be increasing in North America, perhaps reflective of population shifts, climate changes, and genetic susceptibility. Demographic surveys identify up to 20% to 40% of the population as sufferers of AR/conjunctivitis and approximately 8% troubled with asthma.^{1–4}

Allergen immunotherapy (AIT) comes to the forefront in our therapeutic approach to immunoglobulin E (IgE)-mediated diseases (allergic rhinoconjunctivitis, allergic asthma, food allergy, venom sensitivity, and possibly even atopic eczema), as it affords a means of redirecting the untoward immune response, reestablishing immunologic tolerance, and accomplishing long-term clinical remission.

Although effective, current immunotherapy regimens are burdened by tedious treatment regimens that not only negatively impact on patient adherence and compliance but also serve as barriers to limit access to this form of disease-modifying therapy. Furthermore, systemic reactions to immunotherapy, although infrequent, can be severe and potentially life threatening.

Thus, there is a recognized need for newer therapeutic agents that improve the safety of AIT, provide an ease of delivery to patients that fosters compliance and

^a Division of Allergy & Clinical Immunology, Johns Hopkins Medicine, Baltimore, MD 21287, USA; ^b Creticos Research Group, 1300 Saint Paul's Way, Crownsville, MD 21032, USA

E-mail address: psocrates@comcast.net

allows access to a greater proportion of the allergic population that could benefit from this disease-modifying treatment, and achieves an acceptable therapeutic benefit for most patients committing to the course of treatment.

Through the years, various chemical modifications of allergens have been tried in an attempt to enhance efficacy, improve safety, and foster adherence with AIT. In many cases, these previous approaches have been viewed as unsuccessful, or only partially successful, in that the allergenicity and immunogenicity have either decreased, or increased in tandem, with no resultant efficacy/safety benefit ratio realized. However, recent clinical trials have led to promising results in immunization approaches with modified allergens, including immune-stimulatory adjuvants, recombinant allergens, and T-cell-tolerizing constructs, as well as with alternate routes of delivery, including oral and sublingual, intralymphatic, and epicutaneous methods, as vehicles for immunization in allergic respiratory disease^{5–11} (Box 1).

MODIFIED ALLERGEN APPROACHES

Background

Through the years, various groups have attempted to improve AIT through a variety of techniques through which the allergen is modified. In the 1970s to 1980s, efforts by Norman and Marsh at Hopkins modified grass and ragweed (RW) allergens by partially denaturing them in formalin; this led to allergens with markedly reduced allergenicity; but unfortunately, the immunogenicity of allergoids, as judged by the IgG antibody response, was also decreased, as was the clinical effectiveness.^{12,13} Sehon and Lee attempted to modify and decrease allergenicity by coupling the allergens to a polyethylene glycol backbone. Again, the result was the same: allergenicity and immunogenicity decreased together.^{14,15}

Box 1

Modified AIT constructs

Injectable immunotherapy approaches

Alum salts (SQ)

Chemical modifications (SQ)

Allergoids/polymerized allergens

Novel adjuvants (SQ; IM)

DNA vaccines

TLR-9 (CpG oligonucleotides) (SQ)

Linked to allergen; cocombined

Nanoparticle-based VLPs

TLR-4 (MPL) (SQ)

Lysosomal plasmids (IM)

Peptides (T-cell epitopes) (ID)

Recombinant allergens (SQ)

Alternate routes for immunization

Sublingual immunotherapy

Intralymphatic

Epicutaneous

Abbreviations: ID, intradermal; IM, intramuscular; MPL, monophosphoryl lipid A; SQ, subcutaneous; VLPs, viral-like particles.

Download English Version:

<https://daneshyari.com/en/article/3354563>

Download Persian Version:

<https://daneshyari.com/article/3354563>

[Daneshyari.com](https://daneshyari.com)