The immunological basis of food allergies: Mechanisms and emerging treatments.

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Introduction

Food allergies are a growing public health concern, affecting millions worldwide. These allergic reactions occur when the immune system mistakenly identifies a harmless food protein as a threat, leading to a cascade of immune responses. The severity of reactions can range from mild symptoms such as itching and hives to life-threatening anaphylaxis. Understanding the immunological mechanisms behind food allergies is crucial for developing effective treatments and preventive strategies [1].

The immune system plays a pivotal role in food allergies, primarily through an exaggerated response by immunoglobulin E (IgE) antibodies. In allergic individuals, initial exposure to an allergen, such as peanuts or shellfish, triggers sensitization. During this phase, antigen-presenting cells (APCs) process the allergen and present it to naïve T-helper cells (Th2). The Th2 cells release cytokines, including interleukin-4 (IL-4) and interleukin-13 (IL-13), which stimulate B cells to produce allergen-specific IgE antibodies [2].

Once IgE antibodies are produced, they bind to high-affinity receptors (FceRI) on the surface of mast cells and basophils. Upon subsequent exposure to the allergen, cross-linking of IgE molecules leads to degranulation of these immune cells, releasing histamine, prostaglandins, and leukotrienes. These mediators cause the hallmark symptoms of food allergies, such as swelling, difficulty breathing, and gastrointestinal distress [3].

While IgE-mediated food allergies are the most well-known, non-IgE-mediated reactions also contribute to food-related immune responses. These reactions involve T-cell-mediated mechanisms and often present with delayed symptoms, such as eosinophilic esophagitis and food protein-induced enterocolitis syndrome (FPIES). Unlike IgE-mediated allergies, these conditions are more challenging to diagnose and often require biopsy or elimination diets [4].

Genetics play a significant role in the development of food allergies. Children with a family history of atopic diseases, such as asthma or eczema, have a higher risk of developing food allergies. Environmental factors, including dietary changes, antibiotic use, and reduced microbial exposure, have also been implicated in the rising prevalence of food allergies. The "hygiene hypothesis" suggests that reduced exposure to microbes during early childhood skews immune responses toward allergy-prone pathways [5].

Traditional diagnostic methods, such as skin prick tests and serum IgE measurements, are widely used but have limitations in specificity and predictive value. Emerging diagnostic tools include basophil activation tests, microarray-based IgE profiling, and epitope mapping, which offer more precise identification of allergenic components. These advancements aim to improve diagnosis and tailor individualized treatment strategies [6].

One of the most promising advancements in food allergy treatment is immunotherapy. Oral immunotherapy (OIT) involves administering gradually increasing amounts of an allergen to desensitize the immune system. Sublingual immunotherapy (SLIT) and epicutaneous immunotherapy (EPIT) are also being explored as alternative approaches. These therapies aim to retrain the immune system to tolerate allergens with reduced risk of severe reactions [7].

Monoclonal antibodies, such as omalizumab, target IgE and prevent its interaction with mast cells and basophils. Omalizumab has shown promise in reducing allergic reactions and enhancing the effectiveness of immunotherapy. Other biologics, including dupilumab and tezepelumab, are under investigation for their potential to modulate allergic pathways and improve patient outcomes [8].

The gut microbiome plays a critical role in immune regulation and tolerance. Dysbiosis, or an imbalance in gut microbiota, has been linked to increased food allergy susceptibility. Probiotic and prebiotic interventions are being studied as potential therapies to restore microbial balance and promote immune tolerance to allergens [9].

Early introduction of allergenic foods during infancy, as supported by studies such as the LEAP (Learning Early About Peanut) trial, has demonstrated a reduction in food allergy development. Breastfeeding, dietary modifications, and environmental interventions also play a role in prevention strategies [10].

Conclusion

Food allergies involve complex immunological mechanisms, with both IgE-mediated and non-IgE-mediated pathways contributing to their pathophysiology. Advances in

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immunotherapy, biologics, microbiome research, and diagnostic tools offer hope for improved management and potential cures. Ongoing research and public health initiatives are crucial in addressing the rising prevalence of food allergies and improving patient quality of life.

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