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Asthma Immunotherapies: Endotypes, Mechanisms, and Emerging Frontiers

Ryan Quigley:
Welcome to *AudioAbstracts* on ReachMD. I'm Ryan Quigley, and today, I'll be discussing an October 2025 review published in *Cellular and Molecular Immunology,* where investigators examined the immunological underpinnings of asthma endotypes and how these insights are informing the evolution of targeted immunotherapies.

Asthma affects an estimated 260 million people globally. And while there's a growing arsenal of therapies, it continues to account for half a million deaths per year. It's a heterogeneous disease of multiple endotypes, each driven by different immune pathways.

The review outlines two major endotypes: type 2-high asthma, or T2high, and type 2-low asthma, or T2low.

T2high asthma, which accounts for the majority of cases, is driven by Th2 cells and group 2 innate lymphoid cells. These cells release type 2 cytokines, including IL-4, IL-5, IL-9, and IL-13, which promote hallmark features: eosinophilic inflammation, IgE class switching, mucus hypersecretion, features of airway remodeling, and bronchial hyperresponsiveness.

On the other hand, T2low asthma is typically associated with neutrophilic or paucigranulocytic inflammation, Th1/Th17-related cytokines, and inflammasome activation—a profile that tends to respond poorly to corticosteroids.

Importantly, even within these two endotypes, there's substantial biological heterogeneity, reinforcing the need for individualized treatment approaches.

So let's talk about the therapeutic landscape.

Allergen-specific immunotherapy, or AIT for short, is an established form of immunotherapy in allergic T2high asthma, inducing long-term immune tolerance through repeated allergen exposure. While both subcutaneous and sublingual routes have shown clinical benefit, AIT's utility is limited by lengthy treatment duration and risk of adverse reactions.

More recently, biologic therapies offer targeted alternatives for patients with severe or corticosteroid-refractory asthma. Agents like omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab selectively target type 2 inflammatory pathways, with demonstrated reductions in exacerbations, improved lung function, and decreased corticosteroid use. Notably, tezepelumab's efficacy across both T2high and T2low asthma underscores the promise of upstream targets.

Looking ahead, emerging strategies, including long-acting biologics, combination approaches, and CAR-T cell therapy, highlight the potential for more durable, and possibly curative, immunomodulation.

This has been an *AudioAbstract*, and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!

Reference

Hammad H, Ahmed E, Lambrecht BN. Immunotherapy for asthma. *Cell Mol Immunol*. 2025;22(12):1521-1532. doi:10.1038/s41423-025-01357-9.