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Newfound Immune Cells Are Key to Long-Lasting Allergies

Scientists have long sought to understand why allergies linger in our bodies. A new discovery points the way toward improved treatments.

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FOR DECADES, scientists have struggled to unlock one of the biggest enigmas behind allergies — why they don't just go away. How they get started has long been understood. The immune system mistakenly overreacts to a harmless substance, producing antibodies known as immunoglobulin E (IgE). Those antibodies signal immune cells to attack the supposed invader with inflammatory chemicals, resulting in symptoms ranging from mild sniffles to potentially deadly anaphylactic shock. But how does the body remember what it's allergic to so that it produces IgE whenever exposure recurs?

In February, two groups of researchers revealed the keeper of that crucial data: a previously undetected type of memory B cell.

Ordinary memory B cells produce IgG antibodies, which help the immune system recognize antigens such as bacteria and viruses. Although previous studies suggested that a subset of memory B cells could switch to churning out IgE (normally deployed to mark parasitic worms for destruction), their precise identity remained unknown.

To solve the puzzle, both teams used advanced techniques such as singlecell RNA sequencing, which measures gene expression levels in individual cells. At McMaster University in Ontario, researchers led by immunologist Joshua Koenig scrutinized over 90,000 memory B cells from 15 people — six with birch allergies, four with dust mite allergies, and five with no allergies. The team identified a small cohort of memory B cells, dubbed MBC2s, that make the IgE antibodies and proteins associated with allergic reactions.

IN ANOTHER experiment, Koenig and his colleagues collected MBC2s from people with peanut allergies. The cells increased in number and produced IgE antibodies, the researchers found, when those study participants started therapy to desensitize them to peanut allergens. "That's direct evidence that these cells are what keeps you allergic," Koenig says.

The second team, led by Maria Curotto de Lafaille, an immunologist at New York City's Icahn School of Medicine, determined that similar cells — which her group called type 2 memory B cells — were more plentiful in 58 children allergic to peanuts than in 13 nonallergic kids. Lafaille's team also found that these cells switched from producing IgG to IgE after encountering peanut antigens, confirming

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their central role in initiating allergic reactions. The results of both studies, published in Science Translational Medicine, point toward new approaches for treating allergies.

Current methods rely either on controlled exposure to specific allergens — a laborious process that can itself trigger potentially dangerous allergic reactions — or injections of the immunosuppressant drug omalizumab, which can cause harmful side effects. Drugs aimed at the newfound B cells, experts suggest, could be safer and more effective than those options.

"The question now is how to push these cells away from producing IgE," explains Northwestern University allergist and immunologist Cecilia Berin. "That would allow us to target the underlying cause of the disease rather than just suppressing symptoms."