

Discovery could lead to new treatments for life-threatening allergic reactions

ASU researchers probe how the gut responds to severe food allergies

By Richard Harth, ASU News
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Food allergies affect more than half a billion people worldwide. In severe cases, even a small bite of the wrong food can trigger anaphylaxis — a rapid, body-wide allergic reaction that can cause difficulty breathing, a dangerous drop in blood pressure and even death.

Scientists have long understood how injected allergens — like those in lab tests or insect stings — trigger anaphylaxis. But researchers have puzzled over how anaphylaxis begins in the gut after eating a food allergen.

Now, Arizona State University researchers, in collaboration with a team led by Yale University and other partners, have pinpointed a surprising culprit: specialized immune cells in the intestine that produce powerful chemical messengers.

These chemical messengers can cause muscles in the airways and gut to contract, increase mucus production and boost inflammation. They're already known to play a role in asthma attacks. This study¹ shows they are also key drivers of severe food allergy reactions that start in the gut.

[The findings](#), published in the current issue of *Science*, reveal that reactions to allergens in the gut are fundamentally different from reactions to allergens entering the bloodstream directly.

“Until now, we assumed that anaphylaxis followed the same pathway regardless of where allergens entered the body, with histamine from mast cells as the main driver,” says ASU researcher [Esther Borges Florsheim](#). “Our study shows that when allergens are ingested, a specialized set of mast cells in the gut don’t release histamine — instead, they produce lipid-based molecules called leukotrienes. These molecules, rather than histamine, trigger anaphylaxis in the gastrointestinal tract.”

Florsheim is a researcher with the [Biodesign Center for Health Through Microbiomes](#) and assistant professor with the [School of Life Sciences](#) at ASU.

Different path to the same dangerous outcome

In both food and systemic allergies, immune cells called mast cells play a central role. When these cells detect an allergen via antibodies called immunoglobulin E, or IgE, they burst open, releasing chemicals that cause swelling, low blood pressure and other symptoms.

In the bloodstream, the most important of these chemicals is histamine, which is why antihistamines can help in some allergic situations. However, the new research shows that when an allergen is ingested, mast cells in the intestinal lining respond differently. They make relatively little histamine. Instead, they ramp up production of cysteinyl leukotrienes, a family of inflammatory lipids already known to constrict airways in conditions like asthma.

In the gut lining, intestinal mast cells take cues from nearby epithelial cells. These cues shift the cells' activity, so they make more leukotrienes and less histamine. Detailed genetic and chemical analyses showed that intestinal mast cells come in several subtypes. Compared to mast cells elsewhere in the body, mast cells in the gut were primed to make leukotrienes.

Previous research found that blocking the IgE pathway — either by removing IgE antibodies or the receptor they bind to on mast cells — protected against developing severe symptoms.

A new way to prevent food allergy emergencies

To test whether leukotrienes were truly driving the reaction, the team used zileuton, an FDA-approved drug used to treat asthma, which blocks a crucial enzyme needed to make leukotrienes.

The results showed the drug reduced allergy symptoms and provided protection from a dangerous drop in body temperature — a hallmark of anaphylaxis.

Importantly, the same drug did not prevent reactions caused by allergens injected into the bloodstream. That finding showed that the gut pathway is different from the whole-body allergic pathway and has its own chemical drivers.

Current emergency treatments for severe allergic reactions, such as epinephrine, are aimed at quickly reversing symptoms once anaphylaxis starts. Antihistamines can help in mild reactions, but they are far less effective for preventing severe events — especially those triggered by food.

Why this research matters

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The new findings suggest that targeting leukotrienes could offer a new preventive or therapeutic approach for food-triggered anaphylaxis.

More research is still needed to test whether the results from this study can be applied to humans. However, drugs that block leukotriene production (like zileuton) or leukotriene receptors (such as montelukast, also commonly used for asthma) are already approved for other uses, which could speed up testing for food allergy applications.

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More than just a gut reaction

Beyond the potential clinical applications, the work changes how scientists think about allergic reactions. It shows that how an allergen gets into the body — through the skin, bloodstream or gut — can shape the type of immune response involved.

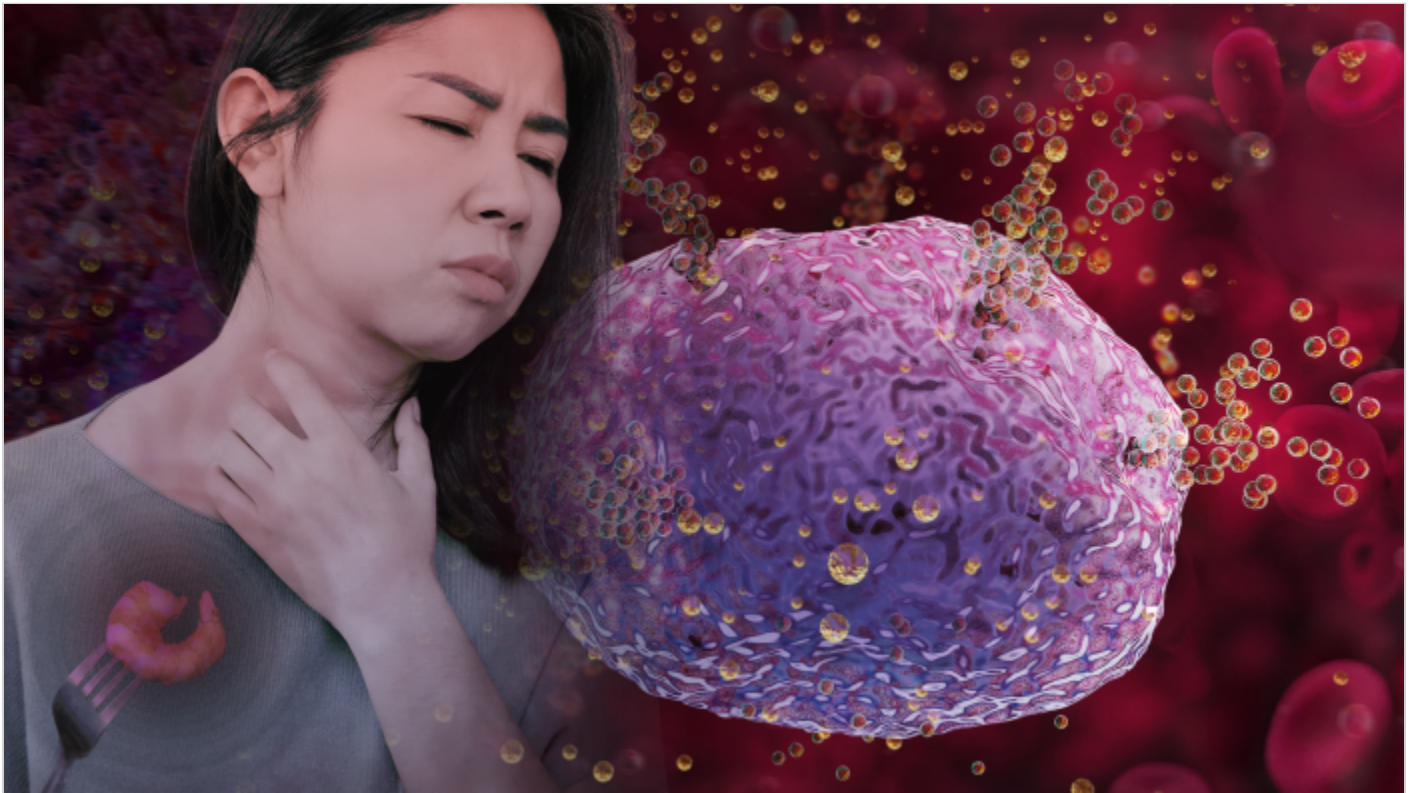
“This finding highlights the gut as unique in how it senses allergens and potentially other harmful environmental challenges, such as food additives,” Florsheim says. “It also helps explain a long-standing puzzle: why levels of food-specific antibodies, especially IgE, do not reliably predict the risk of food allergy.”

The researchers plan to follow up by studying whether similar mast cell populations and leukotriene-driven pathways exist in human intestines, and whether blocking them can reduce or prevent severe reactions in people with life-threatening food allergies.

This story originally appeared on [ASU News](#).

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Main image



Until recently, scientists had little insight into why food allergens can provoke such a dangerous chain reaction in the body. A new study has uncovered an unexpected source: immune cells in the gut that release potent chemical signals capable of setting off anaphylaxis. Graphic by Jason Drees

Text image(s)



Esther Borges Florsheim