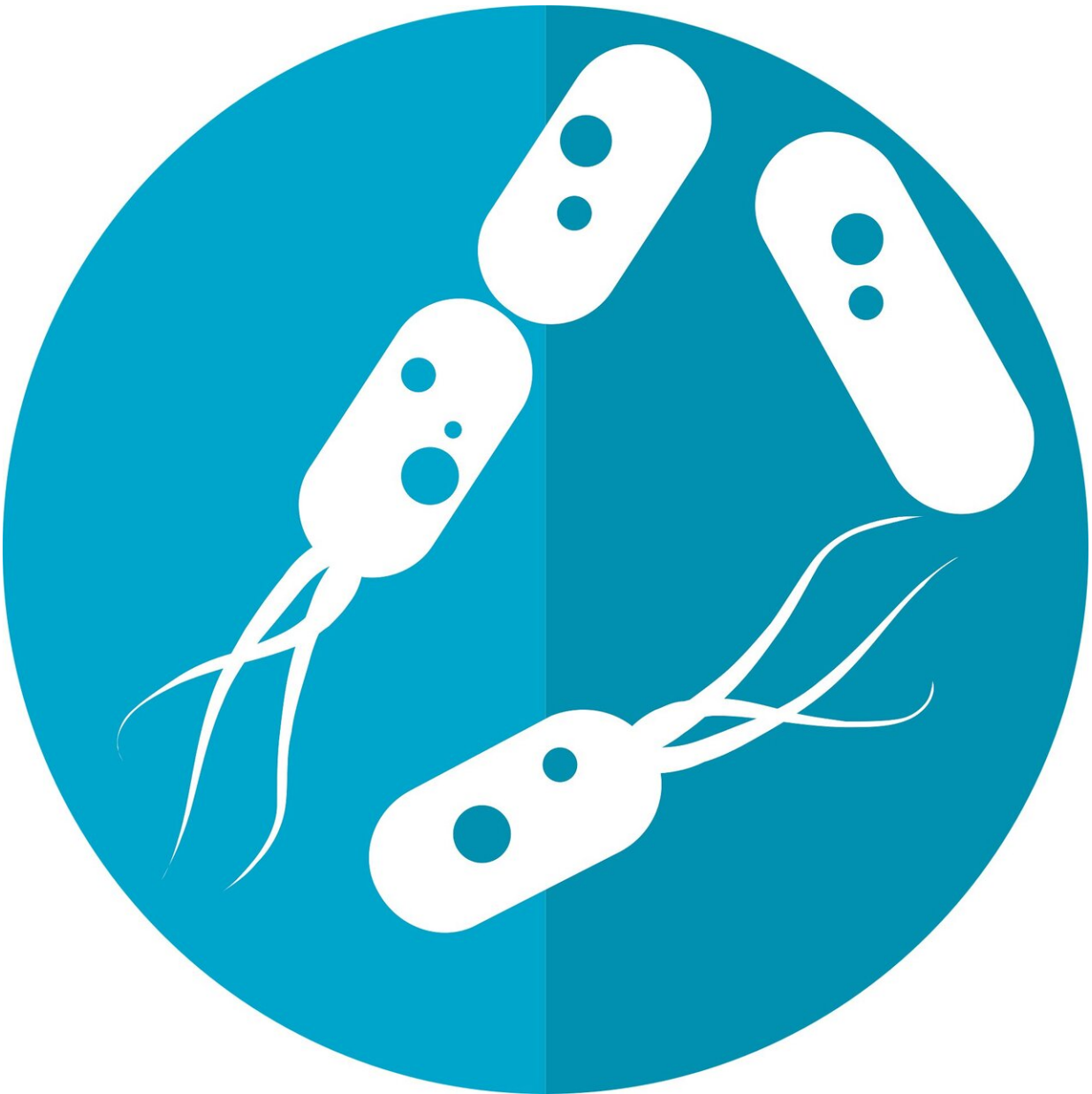


New therapy targets gut bacteria to prevent and reverse food allergies

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Every three minutes, a food-related allergic reaction sends someone to the emergency room in the U.S. Currently, the only way to prevent a reaction is for people with food allergies to completely avoid the food to which they are allergic. Researchers are actively seeking new treatments to prevent or reverse food allergies in patients. Recent insights about the microbiome—the complex ecosystem of microorganisms that live in the gut and other body sites—have suggested that an altered gut microbiome may play a pivotal role in the development of food allergies. A new study, led by investigators from Brigham and Women's Hospital and Boston Children's Hospital, identifies the species of bacteria in the human infant gut that protect against food allergies, finding changes associated with the development of food allergies and an altered immune response. In preclinical studies in a mouse model of food allergy, the team found that giving an enriched oral formulation of five or six species of bacteria found in the human gut protected against food allergies and reversed established disease by reinforcing tolerance of food allergens. The team's results are published in *Nature Medicine*.

"This represents a sea change in our approach to therapeutics for food allergies," said co-senior author Lynn Bry, MD, Ph.D., director of the Massachusetts Host-Microbiome Center at the Brigham. "We've identified the microbes that are associated with protection and ones that are associated with food allergies in patients. If we administer defined consortia representing the protective microbes as a therapeutic, not only can we prevent food allergies from happening, but we can reverse existing food allergies in preclinical models. With these microbes, we are resetting the [immune system](#)."

The research team conducted studies in both humans and preclinical

models to understand the key bacterial species involved in food allergies. The team repeatedly collected fecal samples every four to six months from 56 infants who developed food allergies, finding many differences when comparing their microbiota to 98 infants who did not develop food allergies. Fecal microbiota samples from infants with or without food allergies were transplanted into mice who were sensitized to eggs. Mice who received microbiota from healthy controls were more protected against egg [allergy](#) than those who received microbiota from the infants with food allergies.

Using computational approaches, researchers analyzed differences in the microbes of children with food allergies compared to those without in order to identify microbes associated with protection or food allergies in patients. The team tested to see if orally administering protective microbes to mice could prevent the development of food allergies. They developed two consortia of bacteria that were protective. Two separate consortia of five or six species of bacteria derived from the human gut that belong to species within the Clostridiales or the Bacteroidetes could suppress food allergies in the mouse model, fully protecting the mice and keeping them resistant to egg allergy. Giving other [species of bacteria](#) did not provide protection.

"It's very complicated to look at all of the microbes in the gut and make sense of what they may be doing in food allergy, but by using [computational approaches](#), we were able to narrow in on a specific group of microbes that are associated with a protective effect," said co-first author Georg Gerber, MD, Ph.D., MPH, co-director of the Massachusetts Host-Microbiome Center and chief of the Division of Computational Pathology in the Department of Pathology at the Brigham. "Being able to drill down from hundreds of microbial species to just five or six or so has implications for therapeutics and, from a basic science perspective, means that we can start to figure out how these specific bacteria are conferring protection."

To understand how the bacteria species might be influencing food allergy susceptibility, the team also looked at immunological changes, both in the human infants and in mice. They found that the Clostridiales and Bacteroidetes consortia targeted two important immunological pathways and stimulated specific regulatory T cells, a class of cells that modulate the immune system, changing their profile to promote tolerant responses instead of allergic responses. These effects were found both in the pre-clinical models and also found to occur in human infants.

The new approach represents a marked contrast to oral immunotherapy, a strategy that aims to increase the threshold for triggering an allergic reaction by giving an individual small but increasing amounts of a food allergen. Unlike this approach, the bacteriotherapy changes the immune system's wiring in an allergen-independent fashion, with potential to broadly treat food allergies rather than desensitizing an individual to a specific allergen.

"When you can get down to a mechanistic understanding of what microbes, microbial products, and targets on the patient side are involved, not only are you doing great science, but it also opens up the opportunity for finding a better therapeutic and a better diagnostic approach to disease. With food allergies, this has given us a credible therapeutic that we can now take forward for patient care," said Bry.

Bry and Gerber, along with senior author Talal Chatila, MD, of Boston Children's Hospital, are founders and have equity in ConsortiaTX, a company that is developing a live human biotherapeutic product (CTX-944). (Co-senior author Rima Rachid, MD, of Boston Children's Hospital, also has equity in the company.) ConsortiaTX is preparing for a Phase 1b trial in pediatric food allergy, followed by expansion into additional allergic diseases. ConsortiaTX has obtained an exclusive global license to the intellectual property related to the microbial discoveries published in the *Nature Medicine* paper.

More information: Microbiota therapy acts via a regulatory T cell MyD88/ROR γ t pathway to suppress food allergy, *Nature Medicine* (2019). DOI: [10.1038/s41591-019-0461-z](https://doi.org/10.1038/s41591-019-0461-z) , www.nature.com/articles/s41591-019-0461-z

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