Animal study shows how to retrain the immune system to ease food allergies

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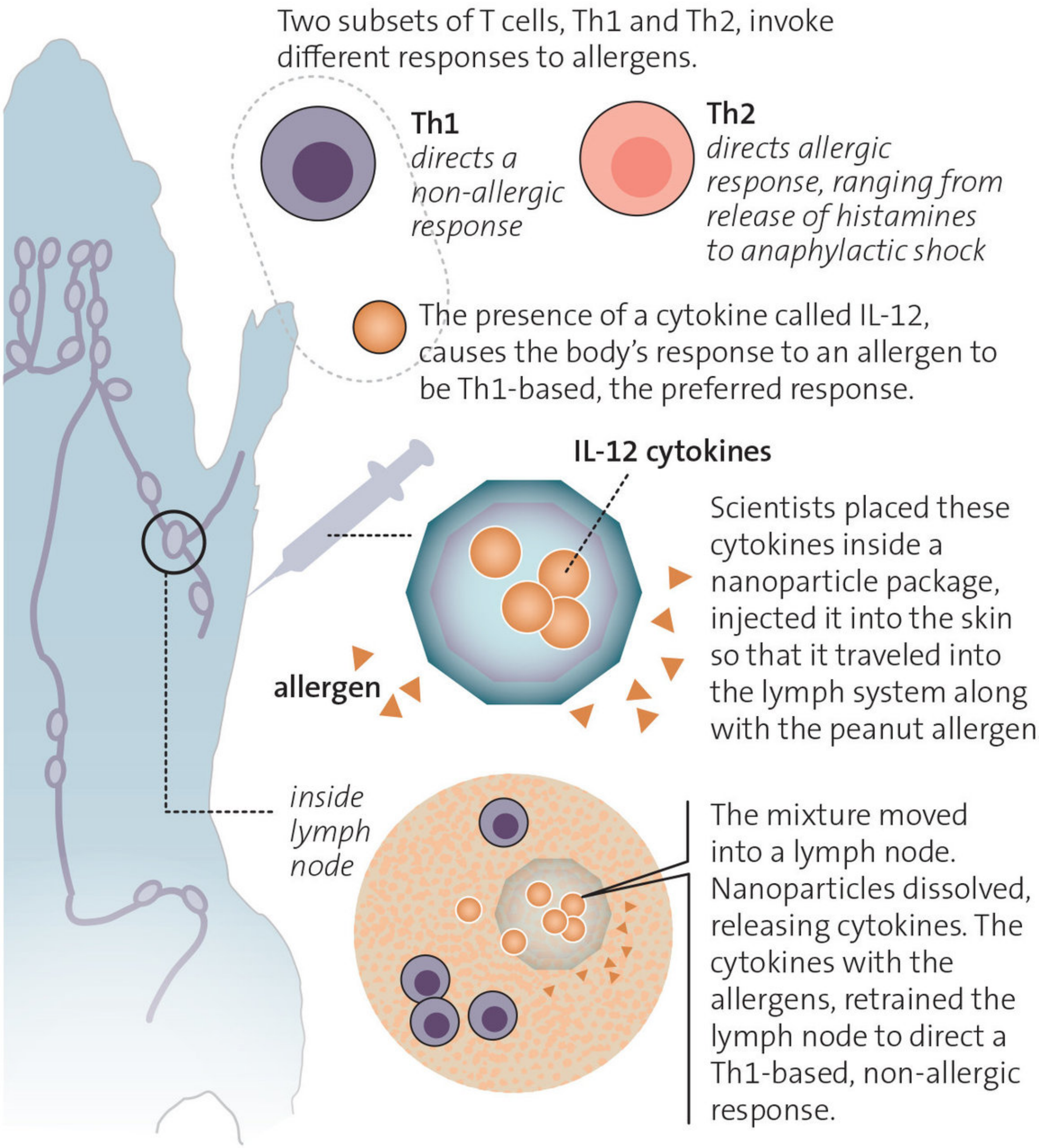
Changing the body's response to a common allergen

Duke scientists have successfully modified the allergic reaction to the peanut allergen in mouse models. Here's their approach:



Alisa Weigandt for Duke Health

DukeHealth

Duke scientists have successfully modified the allergic reaction to the peanut allergen in mouse models. Credit: Alisa Weigandt for Duke Health

Treating food allergies might be a simple matter of teaching the immune system a new trick, researchers at Duke Health have found.

In a study using mice bred to have peanut allergies, the Duke researchers were able to reprogram the animals' immune systems using a nanoparticle delivery of molecules to the lymph nodes that switched off the life-threatening reactions to peanut exposures.

"This study in mice proves the concept of this approach, so tests in humans are not that far off," said Soman N. Abraham, Ph.D., professor in Duke's Department of Pathology. Abraham is senior author of a study published this month in the *Journal of Allergy and Clinical Immunology*.

Food allergies affect an estimated 4 percent of adults in the United States, and up to 6 percent of children. Peanuts are among the most common allergen and can trigger a life-threatening immune response, so people must learn to be vigilant about hidden exposures in everyday food choices.

In recent years, efforts have been made to desensitize allergic people to peanuts and other foods with a series of measured exposures that are gradually increased over time. Such treatments can be effective, but they're also risky and time-consuming.

The approach—planned by lead author Ashley St. John, Ph.D., an assistant professor at the Duke-NUS Medical School in Singapore—appears to resolve those issues.

Starting with the observation that allergic reactions basically result from an imbalance of key messages between cells, called cytokines, the researchers set out to devise a way to restore order.

They focused on the Th2-type cytokine immune response, which is increasingly understood as a driver of the overactive immune responses in allergy attacks. In an appropriate immune response, Th2 works in tandem with Th1, but during allergic reactions, Th2 is overproduced and Th1 is diminished.

The solution appears simple enough: deliver more Th1-type cytokines ahead of an allergen exposure to restore balance. But it has proven difficult. A test of this type was attempted as an asthma therapy, but it required a massive dose to the lungs and was ineffective.

In their experiment with the peanut-allergy mice, St. John and colleagues instead delivered antigen- and cytokine-loaded nanoparticles into the skin. The nanoparticles traveled to the lymph nodes, where they dissolved and dispensed their payload at the source of the immune response.

Animals that received this therapy no longer went into an acute allergic response called anaphylaxis when they were subsequently exposed to peanuts. The new-found tolerance was long-lasting, so did not need to be repeated ahead of each exposure to the allergen.

"The Th1 and Th2 sides of immunity balance each other," St. John said. "We reasoned that since we know Th2 immunity is over-produced during allergic responses, why not try to skew the immune response back the other direction? By delivering cytokines to the lymph nodes where immune responses are established, we were able to re-educate the immune system that an allergic response is not an appropriate one."

The approach could theoretically be applied to other allergens, including environmental triggers such as dust and pollen. Additional experiments are underway to move the findings into human trials.

"We are encouraged by these findings, because it's a fairly simple way to reprogram the immune system," Abraham said.

Provided by Duke University Medical Center

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