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New cell type may help explain why some people have dangerous food allergies

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Researchers have discovered a new cell type that appears to drive life-threatening food allergies and may help explain why some people get severe allergic reactions and others do not.

Reporting their study data Sept. 22 in the journal *Immunity*, scientists at Cincinnati Children's Hospital Medical Center say their findings in mice should also provide insights into new therapeutic strategies and diagnostics for food allergies and anaphylactic shock triggered by the immune antibody IgE (immunoglobulin E).

The authors report discovery of what they call "IL-9-producing mucosal mast cells" or (MMC9 cells). The cells produce large amounts of an inflammatory immune protein called interlukin 9 (IL-9), which amplifies anaphylactic shock in response to ingested food. Prior to this study, the primary cellular source of IL-9 was unknown, according to the authors.

"Our study suggests that although you need to have some level of IgE to trigger a food allergy response, you also have to produce MMC9 cells to get a severe response and anaphylaxis," says Yui-Hsi Wang, PhD, lead investigator and a researcher in the Division of Allergy and Immunology at Cincinnati Children's. "Without these cells you will not get severe food allergies."

Set off by certain foods like peanuts, shell fish and a host of others, IgE-associated food sensitivity prompts the immune systems of some children to surge out of control. Unless there is immediate medical

intervention, this can trigger a molecular chain reaction in the intestines and other organs - leading to diarrhea, hypothermia, respiratory distress and shock.

About 40 percent of children have some IgE-associated food sensitivity, but only 8 percent of the 40 percent develop the severe food reactions that can lead to anaphylactic shock, according to Wang.

"Unfortunately the best medical intervention for these allergies remains avoiding the foods that cause them," he said. "We don't know why some patients develop such a strong response and why some don't. This is where we as basic scientists are coming in to see if we can use mouse models to learn this, because mice are very much like humans."

Wang and his colleagues suspect that some people are wired genetically to have higher or lower susceptibility to severe IgE-related allergic reactions. Still, it also remains unknown exactly how genetics contributes to these molecular chain reactions.

Just as people with food allergies have different degrees of susceptibility, so do mice. To account for this, the researchers conducted their study in several distinct strains of genetically bred mice. They gave the mice an egg white protein called ovalbumin to trigger allergic reactions and study biological reactions in the animals.

They observed that after allergic sensitization, some mouse strains generated large populations of MMC9 cells while other strains did not. Mice that did not produce MMC9 cells exhibited only minor allergic responses. Mice that produced intestinal MMC9 cells all had severe allergic reactions, regardless of whether they had low or high levels of IgE.

Wang and his colleagues report that production of MMC9 cells required

the presence of type-2 CD4+ T helper immune cells and the proteins interlukin-4 and STAT6. By producing significant amounts of IL-9, the MMC9 cells caused mastocytosis and the production of mast cells, which may migrate out of the intestines to other organs as they secrete histamines and other molecules that cause anaphylaxis.

To verify that MMC9 cells were fueling severe allergic reactions in the mice, the researchers treated the mice with an antibody (anti-Fc RImAb), which eliminated the cells and decreased food allergy symptoms. When MMC9 cells were transferred back into the same mice, the animals resumed exhibiting food allergy symptoms.

Researchers next conducted tests to see if their identification of MMC9 cells was relevant to the development of human food allergies. Analyzing small intestine biopsy samples from food allergy patients (who gave authorized consent) the scientists looked for molecular signatures of MMC9 cells. They found significantly increased expression of the Il9 genetic transcript and other related transcripts in the samples of food allergy patients, suggesting a possible connection.

Wang said the researchers are now trying to find the human equivalent (orthologue) of the MMC9 cells they found in their mouse models. One goal the researchers have is to identify that cell and its biological mediators to see if it possible to develop a biomarker that might allow development of a blood test for food allergies. Eventually, Wang said, the team wants to develop a blood test that would allow clinicians to determine which patients are at higher risk for severe food allergies, and to find improved treatments for food allergy.

Provided by Cincinnati Children's Hospital Medical Center