Immune cells hold their memory of how to respond to allergens in a surprising way

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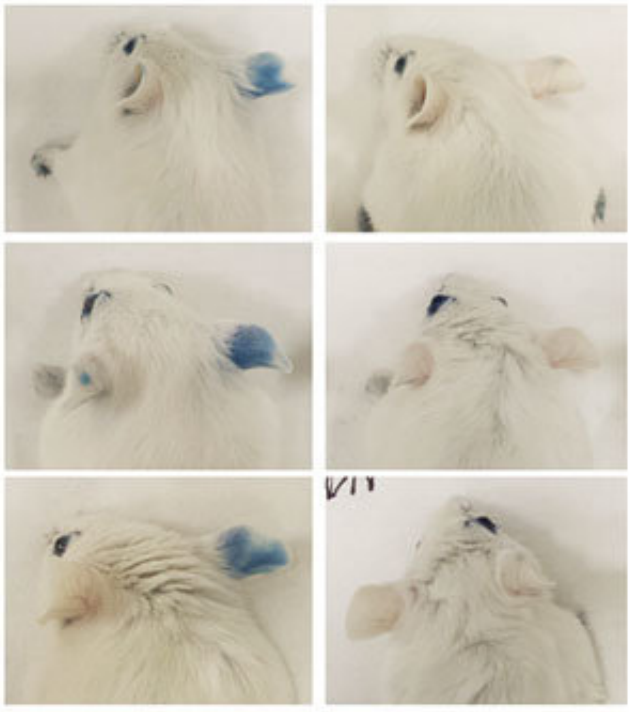

Previously unexposed mice were first injected in their right ears with DP or DN IgG1 B cells and then they were intravenously injected with an antigen. Those injected with DP, on the left, showed a local anaphylactic reaction in their ear (blue). Those injected with DN, on the right, did not. This demonstrates that only the DP cells are producing high affinity IgE. Credit: J. He et al.

Understanding how the immune system remembers allergy-causing antigens could help prevent severe reactions.

When a predisposed person is initially exposed to an allergy-causing antigen, specific antibodies, called immunoglobulin E (IgE), are produced without leading to an allergic reaction. But if exposed to the allergen a second time, the person may become ill. "But no-one has found the memory IgE cells believed to be responsible for the illness," says bioinformatics researcher and molecular viral epidemiologist Michael Poidinger from A*STAR's Singapore Immunology Network (SigN).

Jin-Shu He and colleagues at SigN collaborated with researchers in Singapore and the US to decipher the function of IgE memory. Instead of finding IgE memory cells, they discovered that the memory cells of immunoglobulin G1 (IgG1), another antibody, held the memory of IgE responses.

The team injected mice with one of two antigens, eliciting a primary allergic immune response. They then isolated a type of immune cell from the mice's serum, called memory B cell, specific to IgG1. They found three subsets of this memory B cell: double positive (DP), single positive (SP) and double negative (DN) depending on the types of receptors on their surface. These cells were then injected into mice that hadn't been previously exposed to the antigens; one of the two antigens was administered, and a secondary allergic immune response occurred.

The researchers found that DP IgG1 memory B cells from the donor mice—those that held the memory for either of the two antigens—produced, as expected, a type of white blood cells called plasma cells in the recipient mice, which secreted IgG1 antigen-specific antibodies. Surprisingly, however, they also generated plasma cells that secreted IgE with a high affinity for their specific antigen.

SP and DN IgG1 memory B cells also produced IgE-secreting plasma cells. But the secreted IgE had only a low affinity for their antigens.

It remains unknown what causes the same DP IgG1 memory B cells to generate IgG1 or IgE plasma cells. But the study reveals that IgG1 memory B cell subsets are important in the memory of IgE responses.

In a secondary allergic reaction, allergens bind to IgE attached to the surface of another type of white blood cells, called mast cells, which then release chemicals to cause anaphylaxis. The team hypothesize that low affinity IgE compete with high affinity IgE for space on the surface of mast cells, and may help limit severe allergic reactions.

"This is an early phase study for this aspect of IgE and allergy," says Poidinger. "Knowing how IgE memory is generated, we can ask questions about drugs and preventative treatments."

More information: Jin-Shu He et al. IgG1 memory B cells keep the memory of IgE responses, *Nature Communications* (2017). DOI: 10.1038/s41467-017-00723-0

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