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How the body stops the type 2 innate immune response from triggering allergic disease

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The innate immune response, which is the body's non-specific response to pathogens, was once believed to be a simple system relying on short-lived effector cells alone, but it is now known to be more complex, involving long-lived lymphoid cells. Researchers from the RIKEN Center for Integrative Medical Sciences (IMS) in Japan have now shown how the body suppresses the activation of the long-lived cells after infection, preventing the response for continuing when it is no longer needed.

Parasitic worms, known as helminths, are a formidable challenge to human health, being a major cause of mortality in the developing world. The body's key defense against these parasites and some fungal infections, called the type 2 innate immune response, actually turns out to be a double-edged sword, as it has been implicated in allergic inflammatory responses such as asthma caused by fungal infections.

"This immune response is important, but also can be dangerous if it lasts beyond its necessity," says Kazuyo Moro, team leader of the Laboratory for Innate Immune Systems in IMS, "It was once believed that the response was mainly mounted by short-lived cells, but now we know that it also involves a population of longer-lived innate lymphoid cells. Since a continuing response is associated with allergic inflammation, it is important for us to understand how these cells are turned off."

A key finding of the study, published in *Nature Immunology*, are that these innate lymphoid cells can be shut off by certain cytokine

chemicals—interferon-beta, gamma and interleukin-27—to end the immune response and ensure that the inflammation does not last. In addition, the scientists helped clear up a mystery about these cells by showing that they do not circulate to tissues that require an immune response but are actually located in the tissues, and are only turned on when a threat is detected. "This shows," says Moro, "that the response is mounted in a very locally specific way. This may be another way for the body to prevent the lasting inflammation that can be associated with the response."

According to Shigeo Koyasu, group director of the Laboratory for Immune Cell Systems, who led the group, "These findings are helpful in understanding how the type 2 innate response changes to be both beneficial and harmful. Learning how these cells are activated and inactivated can give us clues for understanding and treating how the body reacts to such infections."

He continues, "We are beginning to gain insights into the innate immune response, which was previously thought to be simpler than our understanding today. I hope that our work will encourage researchers to look for similar regulatory mechanisms in type 1 and type 3 innate immune responses as well, as this will help us to gain a broader understanding of the complexity of our immune response."

More information: Interferon and IL-27 antagonize the function of group 2 innate lymphoid cells and type 2 innate immune responses, DOI: 10.1038/ni.3309

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