



Silencing of molecular 'conversation' may help curb severe allergies

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Scientists in Sydney have identified a process, a synergistic encounter between two molecules, that may account for the extreme allergic reactions some people experience. By silencing at least one of these molecules, it may be possible to treat allergies.

The molecules, IL-4 and IL-21, are cytokines or 'chemical messengers' produced by immune cells known as T cells. T cells use cytokines to communicate with B cells, which then make antibodies. When IL-4 and IL-21 are involved in the same 'conversation' with a B cell, laboratory experiments show they stimulate the production of large amounts of the antibody class known as immunoglobulin E, or IgE.

IgE is a very tightly regulated antibody. Under normal circumstances, it is present in only very small quantities and protects us against parasites. Unfortunately, it becomes damaging when the body makes too much.

The findings, made by Danielle Avery and Dr Stuart Tangye from the Garvan Institute of Medical Research, are now published online in the prestigious international publication *Blood*.

Dr Tangye, a B cell biologist, is interested in understanding how the body regulates the production of antibodies, in this case the IgE class. "IgE is such an efficient molecule that too much of it can be dangerous," he said. "High quantities tend to over-activate other immune cells and it's the action of those other cells that can be damaging. High levels of IgE are associated with allergies including asthma, dermatitis and rhinitis."

"It's been known for many years that IL-4 can drive IgE production in humans and mice. Our finding shows that IL-21 also stimulates production of IgE by human B cells, but it does this by using an entirely different pathway."

"As it happens, the combination of IL-4 and IL-21 provokes a very strong IgE response, around ten times greater than either molecule in isolation."

"Through an ongoing collaboration with Canberra's John Curtin School of Medical Research, Canberra Hospital and Westmead Hospital, we were able to test our theory by looking at patients with mutations in the IL-21 pathway. If you can't activate that pathway, you don't get the synergistic effect between the two cytokines."

"We surmise as a result of this study that it should be possible to target the IL-21 molecule with an antibody to block its ability to activate B cells. This may prove an effective treatment in cases where allergic responses are caused by the synergistic effect of IL-4 and IL-21."

ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Bone, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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