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GARVAN INSTITUTE

Finding suggests novel ways to boost vaccination or natural defences

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Our bodies rely on the production of potent, or 'high affinity', antibodies to fight infection. The process is very complex, yet Sydney scientists have discovered that it hinges on a single molecule, a growth factor, without which it cannot function.

There is much we do not yet understand about our immune system. In simple terms, our bodies produce B cells, which make antibodies, and T cells, which help them. Ways in which these cells operate and interact with each other are still coming to light.

Roughly eight years ago, a new subset of T cells, T follicular helper (TFH) cells, was identified. This important class of T cells operates in specific environments termed 'germinal centres', specialised areas within lymph organs where B cells proliferate to form high affinity antibodies whenever we fight infection. TFH cells play a critical role in that they communicate with, and help activate, B cells.

The novel finding made by Dr Cecile King and PhD student Alexis Vogelzang, from the Garvan Institute of Medical Research in Sydney, was that the molecule interleukin 21 (IL-21) is a growth factor for TFH cells. A paper detailing this finding was published online today in the prestigious international journal *Immunity*.

A cytokine, or chemical messenger, IL-21 is already well known to immunologists. While its newly identified growth factor role is only one of several functions, that function is fundamental. Without IL-21, the all-important TFH cells could neither develop nor survive.

Dr Cecile King, head of the Mucosal Autoimmunity Group at Garvan, has been investigating the roles of IL-21 for several years. "We already knew that IL-21 was produced by TFH cells and that it was a major initiator of proliferation in B cells," she said. "We were surprised to find that TFH cells not only produce IL-21, they also absolutely need it to survive and they utilise it to function."

"We showed that if you take a mouse genetically deficient in IL-21 and immunise it, you don't get TFH cells and you don't get antibody production. Conversely, if you put IL-21 receptor sufficient, or normal, T cells into the same mouse, where of course the B cells remain abnormal, you recover the normal immune reaction."

"These specialised T cells are thought to be the ones that direct traffic. They are the only ones that can move into the B cell zone and initiate high affinity antibody production."

"Without IL-21, we probably wouldn't be completely immunodeficient, just severely compromised. In addition to the high affinity antibodies we're talking about, our bodies also produce a lot of low affinity antibodies for mopping up infection. That low level response happens around-the-clock and is one of our body's first lines of defence."

“You could say that IL-21 directs the most finely-tuned aspect of our immune response. The highly specialised weaponry developed on-the-spot to target aggressive invaders.”

“This finding suggests novel ways to boost vaccination or natural defences.”

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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