



Creating clarity around a key aspect of the immune system

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Australian researchers have made a finding on the frontier of immunology that will create much buzz in the field as it explains how a pivotal class of immune cells, known as T follicular helper cells, is generated.

T follicular helper cells play a central role in helping B cells, one of several kinds of white blood cell in our bodies, make long-lived high-potency antibodies.

Whenever we are infected, or vaccinated, many of our B cells migrate to antibody-generating hot spots in lymph nodes known as 'germinal centres'. T follicular helper cells cluster around germinal centres, communicating with B cells and helping them make the best possible 'antigen-specific' antibodies.

Not only do these antibodies fight the current infection, but 'Memory B cells' created in the process instantly recognise the same invader in the future.

In the course of a lifetime, we develop millions of Memory B cells, which spring into action against many of the common bacteria, viruses and other microbes we encounter. Without them, our immune systems are severely compromised.

T follicular helper cells were discovered around a decade ago, and since then scientists have been trying to work out exactly how they are generated and how they function. Over the last 3 or 4 years in particular, the topic has become very 'sexy' in the world of immunology, with much confusion, even contradiction, in the scientific literature.

Drs Elissa Deenick, Stuart Tangye and Robert Brink from Sydney's Garvan Institute of Medical Research, have just published a paper in one of the most influential immunology journals, *Immunity*, that should help silence at least part of the debate.

"If you don't have T follicular helper cells, you won't have germinal centres, you won't have high affinity antibodies, you won't have memory cells," said Dr Deenick.

"As they're so central, it's important for us to understand exactly how they work. One of the muddiest areas of debate has been how they're generated in the first place, and I believe our findings clarify that."

T follicular helper cells are a specialised subset of T cells – another class of immune cells. To become T follicular helper cells, ordinary T cells must express certain proteins and cell surface receptors that help them migrate to germinal centres, zones from which ordinary T cells are excluded. They must also encounter antigen – the invader.

The prevailing dogma has been that T cells become activated on immune cells known as dendritic cells – which deliver antigen – then migrate to germinal centres where B cells deliver a special chemical signal, allowing them to become T follicular helper cells. This paper has overturned that two-stage dogma.

“Our work shows that the B cell doesn’t send any unique signal to the T cell to help it become a T follicular helper cell – but that dendritic cells can give the T cells all the signals that they need to make the change.”

“The important thing is that antigen needs to be given to a T cell, and that can come from a dendritic cell, a B cell, or any other source.”

“Once in existence, a T follicular helper cell has a very special relationship with B cells, driven by the surface molecules it expresses and chemicals it secretes.”

Senior co-author Dr Stuart Tangye believes the study forms a research milestone. “It’s very important because it explains previously published results around the world that were almost contradictory,” he said.

“It sits in the middle of other people’s studies with a very rational explanation as to why people have got polarised results in the past.”

“In other words, it explains data that people were clutching at straws to explain.”

Future drug and vaccine development relies on us reaching a very clear understanding of how the essential components of the immune system fit together at a molecular level.

To perfect the best vaccines, we must understand the nuts and bolts of antibody generation. To fight autoimmune diseases (where the body attacks itself), we must find ways of subduing the antibodies that attack the self.

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 nearly 500 scientists, students and support staff. Garvan’s main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation and Neuroscience. 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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