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Scientists discover immune peacekeepers

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There are more bacteria living on our skin and in our gut than cells in our body. We need them. But until now no-one knew how the immune system could tell that these bacteria are harmless.

Centenary Institute researchers in Sydney have discovered a set of peacekeepers—immune cells in the outer layers of our skin that stop us from attacking friendly bacteria.

The work will open the way to new therapeutic options for immune-mediated diseases such as inflammatory bowel disease, of which Australia has some of the world's highest rates.

In a paper published today in the *Proceedings of the National Academy of Sciences* (*PNAS*), Professor Barbara Fazekas de St Groth and her team have shown that the immune cells in the outer layer of the skin constantly act as peacekeepers to stop the immune system from reacting the way it normally would. Known as Langerhans cells, they resisted every attempt by the researchers to get them to generate an immune response.

The researchers worked with a group of mice in which only the Langerhans cells could stimulate the immune system. They then activated the Langerhans cells and measured the response.

"No matter what we threw at them to get them to activate a long-term immune response, the Langerhans cells always induced immune tolerance," Prof Fazekas says.

This result seems to go against the prevailing wisdom in immunology about the workings of dendritic cells, the class of immune cell to which Langerhans cells belong.

Dendritic cells engulf bacteria, viruses or other invaders and put a marker from that invader, known as an antigen, on a protein that can bind to other immune cells.

The antigen reprograms passing T cells, the workhorses of the immune system, which then set off a cascade of responses that eventually lead to the destruction of anything displaying that antigen.

However, the Centenary team (which is affiliated with the University of Sydney and RPA Hospital) found Langerhans cells are very different from other dendritic cells: after turning on the helper T cells, they tell them to self-destruct instead.

"This is the opposite of what you'd usually expect. In previous studies of immune cells, if there was a flurry of activity, we assumed it was the start of a long-term immune response," Prof Fazekas says.

However, the immune system is a layered defence—the next layer of skin has different kinds of dendritic cells, which program on-going responses against bacteria. So if bacteria penetrate deep enough to meet these cells, the immune response will kill them.

In inflammatory bowel disease, which afflicts thousands of Australians, the immune system is activated against the gut bacteria, which are usually left alone.

This discovery opens up possible ways to figure out why this disorder occurs and to find treatments to a range of diseases of the immune system.

"There is so much we don't know about the immune system, but sometimes just mimicking what the system does, like we do with vaccines, can work very well" Prof Fazekas says,

"If we do manage to mimic what Langerhans cells do, then we could develop treatments that would precisely tolerise against specific antigens – just like the immune system of the skin does now."

Centenary Institute executive director Professor Mathew Vadas says this latest paper comes just weeks after Centenary researcher Patrick Bertolino made the front cover of *PNAS* for his paper on immune response in the liver.

"The Centenary Institute is interested in understanding how the immune system works—these discoveries and others already in the pipeline here are a major step forward towards that goal," Prof Vadas says.

Provided by Centenary Institute