Enzyme behind immune cell response revealed

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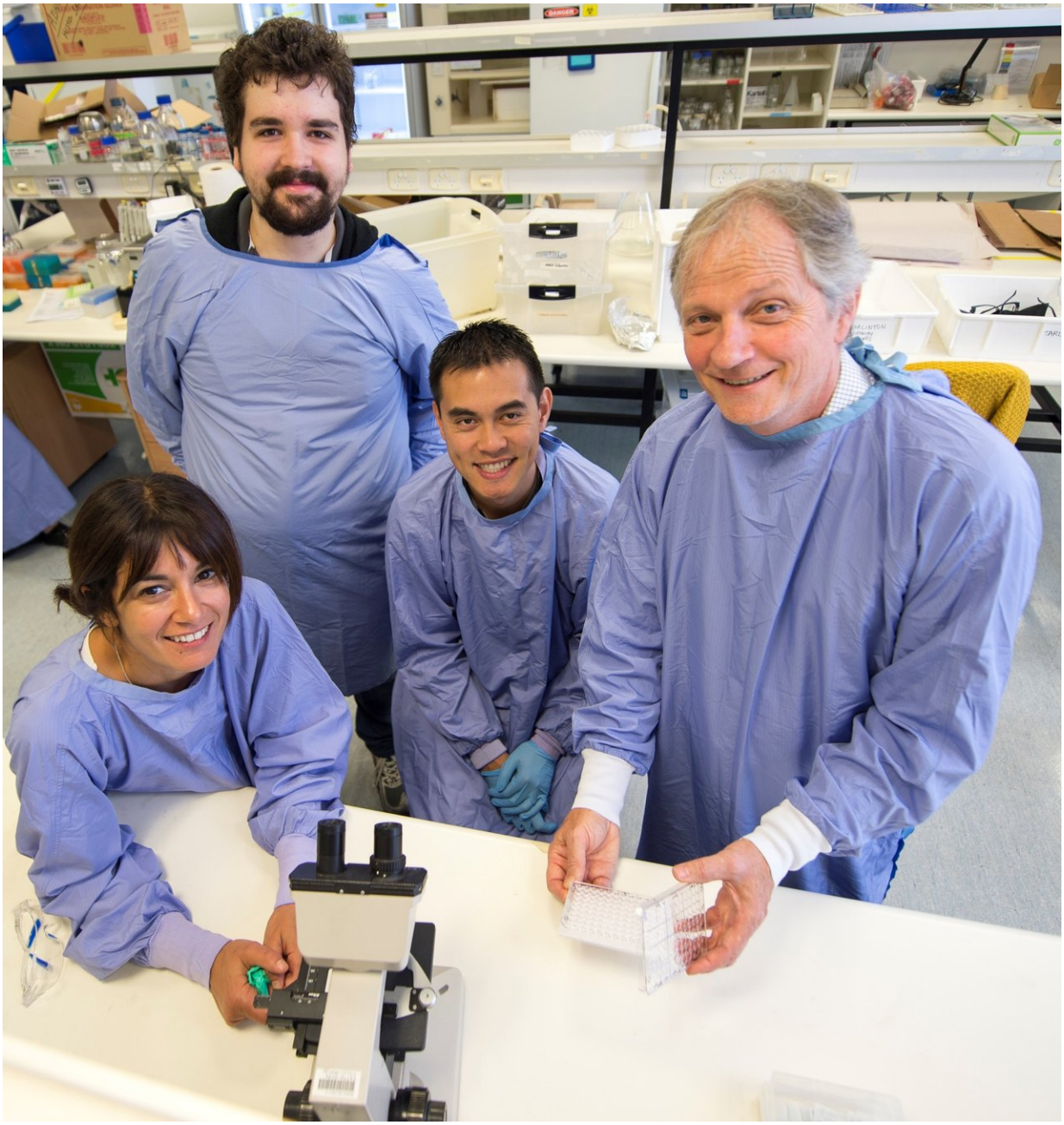

L-R: Dr Simona Infantino, Mr Nick Kocovski, Mr Michael Low, Prof David Tarlinton. Credit: Monash university

Monash University researchers have revealed the role played by an enzyme that is pivotal to the process of clearing infection in the body. Moreover, they suggest that the enzyme may be a potential target for drug development to block the types of inappropriate or excessive cell behaviour that occur in cancer and autoimmunity.

The production of antibodies - proteins secreted into our blood that neutralise invaders such as bacteria and viruses - is one of the immune system's most important ways of protecting us from infections.

But the immune cells that ultimately make or secrete the antibody - a type of white blood cell called B-cells or B-lymphocytes - need to change significantly to do this. They have to be activated, proliferate and change their function, all of which requires significant remodeling of the machinery of the cell.

Researchers from Monash's Central Clinical School led by Professor David Tarlinton, Head of the Immune Memory Laboratory, discovered that an enzyme called PRMT1 is behind this remodeling.

"The cumulative effect of PRMT1 activity in B cells is to make the cells able to sustain the cell division and differentiation that is required to make antibodies," Professor Tarlinton said.

"Without PRMT1 in B cells, there is no antibody production and no way to clear an infection."

The study was published today in *Nature Communications*. First author is Dr Simona Infantino.

The study observed in mice models, an increase in the amount of the enzyme and in its activity - and then observed this in human B cells in a petri dish.

"I think we have very good reason to think and expect that the properties we see in mouse B cells will be repeated in human cells if stimulated in the same way," Professor Tarlinton said.

He said the enzyme had many targets that have previously been identified and found to be important for particular processes, but that it had not been known previously that PRMT1 was required for a complete immune cell response.

"The enzyme is a potential target in the future for blocking this behaviour when it is inappropriate, such as when cells divide and multiply in cancer. It's probably also important for lymphocytes in auto-immune disease," he said. "Any time that you want to suppress immune responses, this would provide an opportunity or a druggable target."

However, such drugs would have many side-effects, he cautioned.

Professor Tarlinton said that preliminary data indicated that the process may be a feature of the way all cells respond to dramatic changes in their environment.

More information: Simona Infantino et al, Arginine methylation catalyzed by PRMT1 is required for B cell activation and differentiation, *Nature Communications* (2017). DOI: 10.1038/s41467-017-01009-1

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