Rare immune cells could hold key to treating immune disorders

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The characterisation of a rare immune cell's involvement in antibody production and ability to 'remember' infectious agents could help to improve vaccination and lead to new treatments for immune disorders, say researchers from the Walter and Eliza Hall Institute.

The cells, called T follicular helper cells, represent less than half of one per cent of all immune cells, but play a critical role in antibody production and developing long-lasting immunity. However, the cells are also dramatically increased in chronic inflammatory disease, suggesting that they could be a therapeutic target for treating these diseases.

The research team, led by Dr Katja Lüthje and Associate Professor David Tarlinton, from the institute's Immunology division, and Dr Stephen Nutt from the institute's Molecular Immunology division, discovered a means of identifying the rare T follicular helper cells while they are actually involved in instructing the immune response, revealing for the first time the possible fates of these cells. The research was published today in the journal *Nature Immunology*.

Dr Lüthje said the research team discovered T follicular helper cells were essential for developing strong and specific antibody responses to infectious agents. "Antibodies are fundamental to the body's defence against infection," Dr Lüthje said. "Antibody production critically relies on the interaction of two cell types: B cells that produce antibody, and helper T cells that recruit and 'teach' the B cells how to respond to infectious agents. In this study, we used a special fluorescent protein to

help identify exactly which cells were involved in the process, and discovered that, amongst the rare T follicular helper cells, only a subset were actively involved in instructing B cells in antibody production."

Dr Nutt said that one of the key findings made by the research team was that T follicular helper cells can remember being exposed to infectious agents, allowing them to rapidly react to subsequent attacks. "The success of vaccines relies on antibody production and long-term immune 'memory'; without these, most routinely-used vaccines, including measles, mumps and tetanus, do not work," Dr Nutt said. "It is well established that antibody-producing B cells can remember a particular infectious agent and rapidly respond if and when they come across it again. Our study shows, for the first time, that T follicular helper cells also develop memory to rapidly respond to infection."

"This finding is incredibly important for the development of vaccines, which relies on immune memory to prevent subsequent infections," Dr Nutt said. "Some vaccines, such as polio are very effective at establishing long-term immunity, while others, such as the cholera vaccine are not particularly effective and need ongoing boosters. It may be that the vaccines are not establishing good T follicular helper cell memory, and this could be something to look at for developing new vaccines for diseases that currently do not have good preventive treatments."

Associate Professor Tarlinton said another key finding was that T follicular helper cells show a remarkable flexibility in their role in immunity. "We found that T follicular helper cells are pretty flexible, adapting to carry out several different functions depending on where they are needed," he said. He said the research team also discovered that T follicular helper cell numbers are tightly controlled by the immune system, which might explain why increases in their numbers are associated with chronic inflammatory diseases, which include

rheumatoid arthritis, type 1 diabetes, lupus and multiple sclerosis.

"In some models, a large increase in the numbers of T follicular helper cells is associated with the development of chronic inflammatory, or what we call autoimmune, diseases in which the immune system attacks its own tissues," Associate Professor Tarlinton said. "In fact, it has been found that T follicular helper cells, in mouse models, were actually the cause of an autoimmune disease very much like lupus in humans. This suggests that modulating these cells could be a potential treatment for autoimmune conditions."

Provided by Walter and Eliza Hall Institute