Newly identified cell population key to immune response

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Dr. Axel Kallies from the Walter and Eliza Hall Institute in Melbourne, Australia, and his colleagues have used molecular signatures to identify a key cell population responsible for regulating the body's immune response. Credit: Walter and Eliza Hall Institute

Scientists from the Walter and Eliza Hall Institute have identified the key immune cell population responsible for regulating the body's immune response.

The finding could have wide-ranging repercussions for the treatment of autoimmune diseases, organ transplantation and cancer, and change how the efficacy of newly developed drugs is measured.

The discovery was made by Dr Erika Cretney, Dr Axel Kallies and Dr Stephen Nutt from the institute's Molecular Immunology division. It

centred on a population of immune cells called regulatory T cells.

Regulatory T cells (T-regs) are responsible for limiting the immune response. Disorders that decrease T-reg activity can lead to autoimmune disorders such as type 1 diabetes or coeliac disease, while increased T-reg activity can suppress the immune system when it should be actively killing cancerous or infected cells.

Dr Kallies said the research team had used molecular signatures to identify which cells within the regulatory T cell population were responsible for suppressing immune responses.

"It turns out that the bulk of cells which are classified as regulatory T cells may not do much," Dr Kallies said. "In this study we have identified a distinct group of effector regulatory T cells, or 'active T-regs', which are the key drivers of immune response regulation."

Dr Nutt said the research had implications for clinical trial outcomes.

"Researchers often measure regulatory T cell numbers in clinical trials as a parameter for establishing whether there has been a positive immune response," Dr Nutt said. "We have shown that the absolute number of regulatory T cells isn't as important as the presence of this particular active regulatory T cell population."

Dr Nutt said the research showed that mice without active T-reg cell populations developed severe autoimmune inflammatory bowel disease, which is fatal.

"Not having this T cell population in the gut causes the immune response to go into overdrive and attack the body's own cells," he said. "A lack of the factor that is needed to generate active T-reg cells has also been implicated in human genome-wide studies of Crohn's disease. So it

would seem that this cell population is strongly linked to the development of autoimmunity."

Dr Cretney said that re-defining the active subset of the T-reg population would give researchers the ability to develop new ways to increase or block their activity in the body. "The next step for my research is to look at the function of this active T-reg population in autoimmunity and in cancer."

Dr Kallies said that for these reasons, there was a lot of excitement in the medical community about regulatory T cells. "Clinicians have shown that regulatory T cell activity impacts on many therapies," he said. "Many research teams are trying to manipulate and expand these cells for therapeutic use. Our finding will transform the way that researchers look at immune responses and open new avenues for treating diseases such as autoimmunity and cancer."

More information: The research appears on the cover of today's edition of *Nature Immunology*.

Provided by Walter and Eliza Hall Institute