Trinity scientists discover new "Jekyll and Hyde" immune cell

Scientists at Trinity College Dublin have identified a rare, new cell in the immune system with "Jekyll and Hyde properties". These cells play a key protective role in immunity to infection but – if unregulated – also mediate tissue damage in autoimmune disorders.

The findings should help us design more effective vaccines to prevent infections such as MRSA, and may also assist help us develop of new therapies for autoimmune diseases, such as multiple sclerosis or rheumatoid arthritis.

The research was funded by Science Foundation Ireland and led by **Kingston Mills**, Professor of Experimental Immunology, and Dr Sarah Edwards and Dr Caroline Sutton, Postdoctoral Fellows in the School of Biochemistry and Immunology in the Trinity Biomedical Sciences Institute. Their findings were published today [**27 February 2020**] in *The Journal of Experimental Medicine.*

The immune system functions to control infection, utilising various immune cells, such as T cells to respond to and control invading microbes. However, if these immune cells are not highly regulated, they can attack and damage body tissues, leading to the development of autoimmune diseases.

Molecules called T cell receptors (TCRs) allow T cells to recognise components of infectious agents with exquisite specificity. The TCRs enable T cells to respond to and eventually eliminate the infectious agent.

Professor Kingston Mills said:

"Until now scientists thought that there were two discrete populations of T cells, expressing either 'αβ' or 'γδ' TCRs. The αβs are the most common T cells in the body. They play a key role in remembering prior infection or immunisation and thereby help protect us against re-infection and mediate vaccine-induced protective immunity. The γδs are more prevalent at mucosal surfaces, such as the lung or gut, and provide an immediate first line of defence against pathogens that invade through these routes."

"We have discovered a new cell type that expresses both αβ and γδ TCRs. This rare population of chimeric or hybrid αβ-γδ T cells has properties of both αβ and γδ T cells. Importantly, they are normally highly activated and poised to act as first responders to control bacterial infection. However, given this high level of activation, they are effectively 'Jekyll and Hyde cells' because in certain contexts they can also precipitate autoimmune responses."

Using a model of *Staphylococcus aureus* infection, Professor Mills and his team found that these cells are rapidly mobilised during infection and play a key role in quickly eliminating the microbes from the body.

The induction of these hybrid αβ-γδ T cells may thus represent a novel approach in the design of more effective vaccines against *Staph aureus* and other infectious diseases, while advancing our ability to control their response may yield additional therapeutic options.

Professor Mills added:

"In a model of autoimmune disease, we found that the hybrid T cells can also trigger the inflammatory cascade that mediates tissue damage in autoimmunity. Therefore, approaches for inhibiting these highly activated immune cells in susceptible individuals may open up new approaches for the treatment of autoimmune diseases such as psoriasis and multiple sclerosis."

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