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What is this research about?

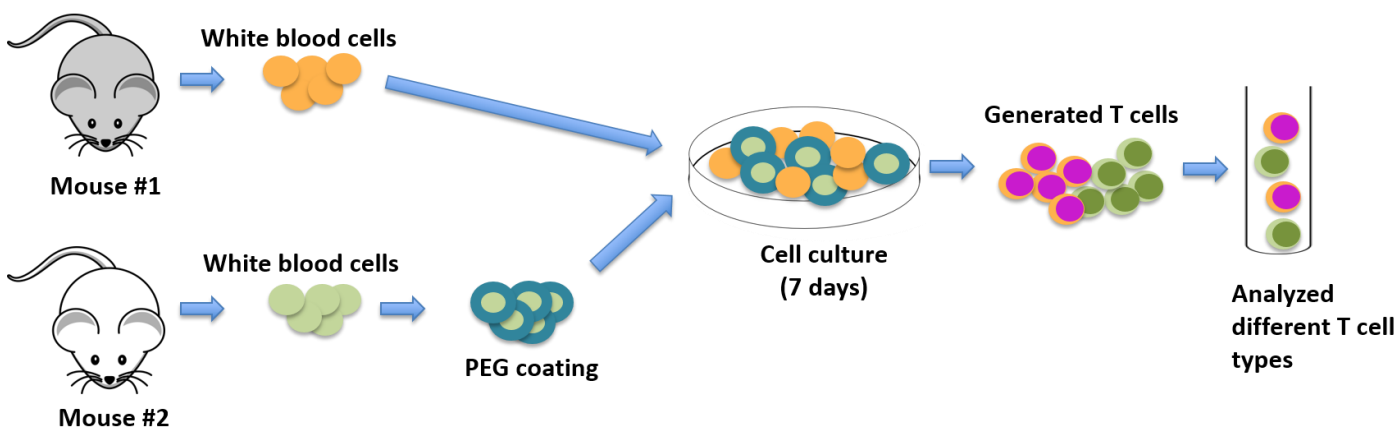
The immune system includes an army of white blood cells that help protect the body from foreign invaders. A T cell is a type of white blood cell that plays a central role in the body's immunity. T cells recognize and react to foreign markers on bacteria and viruses as well as non-self tissues and organs and thus are a significant barrier to successful transplantation of organs and tissues.

The immune response is driven by a process known as antigen presentation. Specialized white blood cells called antigen-presenting cells (APCs) absorb and display foreign markers (called antigens) on their surfaces. T cells interact with the APCs to identify the displayed antigens as non-self. The T cells then become activated, turning into inflammatory cytotoxic (cell-killing) T cells or helper T cells, and start attacking and destroying anything that has those foreign markers. Although this process is important to protect from illness, an uncontrolled inflammatory immune response could harm or even kill the host. The immune system has another T cell type - T regulatory cells (Tregs) - that limits the magnitude and the duration of the immune response by suppressing the production of helper and cytotoxic T cells.

Conventional organ and tissue transplantation therapy uses anti-rejection drugs that decrease the inflammatory response by inhibiting the expansion of the proinflammatory T cells. Although these drugs are necessary to avoid transplant rejection, they have many harmful side effects. In an attempt to prevent these adverse effects, clinical and basic researchers have recently shifted their focus towards enhancing T regulatory cell activity. However, this approach is complex and time consuming, so a simpler approach would be very useful.

Canadian Blood Services' researchers have developed a technique for camouflaging transplanted tissues/organs from the recipient's immune system to increase transplantation success. The antigens can be masked with polyethylene glycol (PEG), a polymer that has been safely used in a variety of drugs and therapies for almost 40 years. This immunocamouflage technique using PEG hides the transplanted cells from the recipient's immune system without affecting the cells' function or their survival in the recipient's body.

What did the researchers do?



In this study, the researchers examined the effect of PEG-coated white blood cells on the generation of different T cells types—cytotoxic T cells, helper T cells and Treg cells. First, the researchers chemically glued PEG to the surface of mouse white blood cells. Next, these PEG-coated mouse white blood cells were mixed

In brief...

A new technique that tricks the immune system could make tissue transplantation safer and more accessible.

with normal (non PEG-coated) white blood cells collected from another mouse. Mixing white blood cells from two different mice causes an immune response and the white blood cells generate different T cell types.

The researchers compared the numbers of different T cells generated with PEG-coated vs. uncoated white blood cells, based on different proteins and markers present on the T cell surfaces.

What did the researchers find?

- ◆ The immunocamouflage technique was highly effective at masking the T cell surface proteins involved in the APC and T cell interactions that are necessary for initiating an inflammatory response.
- ◆ PEG coating of the white blood cells suppressed the production of cytotoxic T cells and helper T cells.
- ◆ PEG coating of the white blood cells increased the production of functional Treg cells that reduce undesired inflammatory response by suppressing the production of cytotoxic and helper T cells.

How can you use this research?

Foreign markers on donor tissues and organs are strong initiators of immune response. This study shows that a PEG polymer coating technique generates functional Treg cells. Treg cells suppress harmful immune responses by inhibiting the production of cytotoxic T cells and helper T cells.

PEG coating of white blood cells could be a useful approach to suppress the unwanted immune response against the transplanted tissues/organs. The recipient's Treg cell population could be increased by injections with PEG-coated white blood cells before and after transplantation. Similarly, PEG-coated white blood cells could be used to treat autoimmune disease patients, whose immune systems attack and damage their own tissues. Increasing the number of Treg cells in these patients could suppress the unwanted inflammatory response.

This polymer coating approach could help prevent transplant rejection without the harmful side effects observed with anti-rejection drugs, increasing transplantation safety. Better understanding of the mechanisms behind the generation of Treg cells via PEG-coating of the white blood cells will help us develop much safer and more effective treatments that reduce unwanted inflammatory responses in tissue/organ transplantation and in autoimmune diseases.

About the research team: This research was conducted in the laboratory of **Dr. Mark Scott**, a senior scientist at Canadian Blood Services' Centre for Innovation and a clinical professor in the department of Pathology and Laboratory Medicine at the University of British Columbia, Vancouver, BC. The lead author, Dr. Ning Kang, is a research associate in Dr. Scott's laboratory. Wendy Toyofuku is a senior research assistant and Xining Yang is a PhD student in Dr. Scott's laboratory.

This ResearchUnit is derived from the following publication:

[1] Kang N, Toyofuku WM, Yang X, Scott MD: Inhibition of allogeneic cytotoxic T cell (CD8⁺) proliferation via polymer-induced Treg (CD4⁺) cells. *Acta Biomater.* 2017; 58:146-155

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