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How to engineer a stronger immune system

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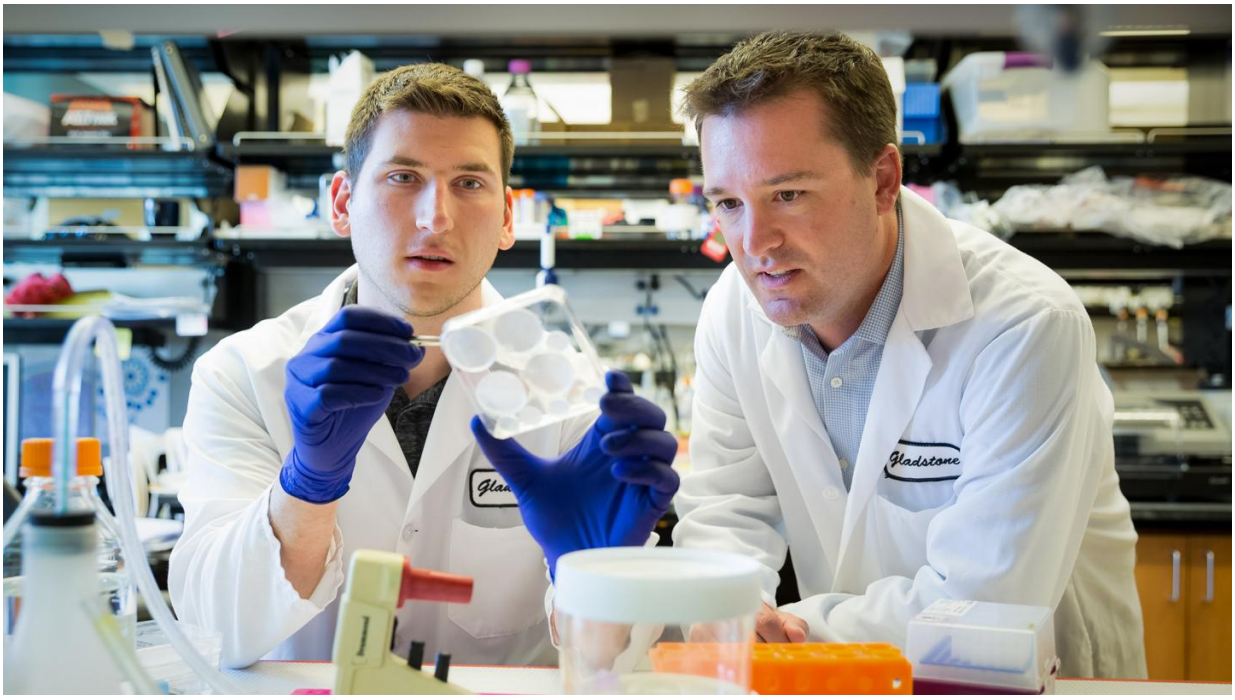

Josh Zimmerman, Ph.D., (right) and Todd McDevitt, Ph.D., discovered a biomaterials hack that can boost cells' ability to combat inflammation and potentially treat autoimmune diseases. Credit: Elisabeth Fall

With a trick of engineering, scientists at the Gladstone Institutes improved a potential weapon against inflammation and autoimmune disorders. Their work could one day benefit patients who suffer from inflammatory bowel disease or organ transplant rejection.

The Body's Natural Defense

Mesenchymal stromal cells (MSCs) reside in bone marrow and have been found to secrete anti-inflammatory proteins that help regulate the immune system. More than 500 clinical trials are trying to use these cells to fight diseases, but so far, many have failed.

Scientists think this failure may be because, like a match needs to be sparked to create a flame, MSCs must be triggered by pro-inflammatory proteins to produce their immune-suppressing effects. Some studies have tried soaking MSCs in a bath of pro-inflammatory chemicals before injecting the cells into a patient. However, the effects are short-lived, wearing off after just a few days.

"The success of therapies involving MSCs depends on the cells' environment," explained Todd McDevitt, PhD, a senior investigator at Gladstone. "A patient taking anti-inflammatory medication may not have high enough levels of inflammation to trigger the cells. We engineered the MSCs to ensure that they are consistently activated, so they can reliably dampen the immune response for longer."

Engineering A Better Method

In the new study, published in *Stem Cells Translational Medicine*, the scientists engineered tiny sugar-based particles that they loaded with pro-inflammatory proteins and stuck into the middle of clusters of MSCs. The particles slowly delivered the inflammatory trigger to the cells in a steady dose. This method increased the amount of anti-inflammatory proteins produced by the MSCs, enhancing the suppression of immune cells. In short, the cell-protein packets worked better and longer than other treatments.

"No one has successfully used biomaterials to deliver pro-inflammatory signals to control how MSCs affect the immune system," said first author Josh Zimmerman, PhD, a former graduate student in the McDevitt lab. "Our research suggests bioengineering has real potential to improve the anti-inflammatory and therapeutic abilities of MSCs. The next step is to test this method in a mouse model of autoimmune disease."

More information: J. A. Zimmermann et al, Enhanced Immunosuppression of T Cells by Sustained Presentation of Bioactive Interferon- Within Three-Dimensional Mesenchymal Stem Cell Constructs, *Stem Cells Translational Medicine* (2016). DOI: 10.5966/sctm.2016-0044

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