Researchers develop preclinical vaccine to regulate immune responses to prevent kidney and heart transplant rejection

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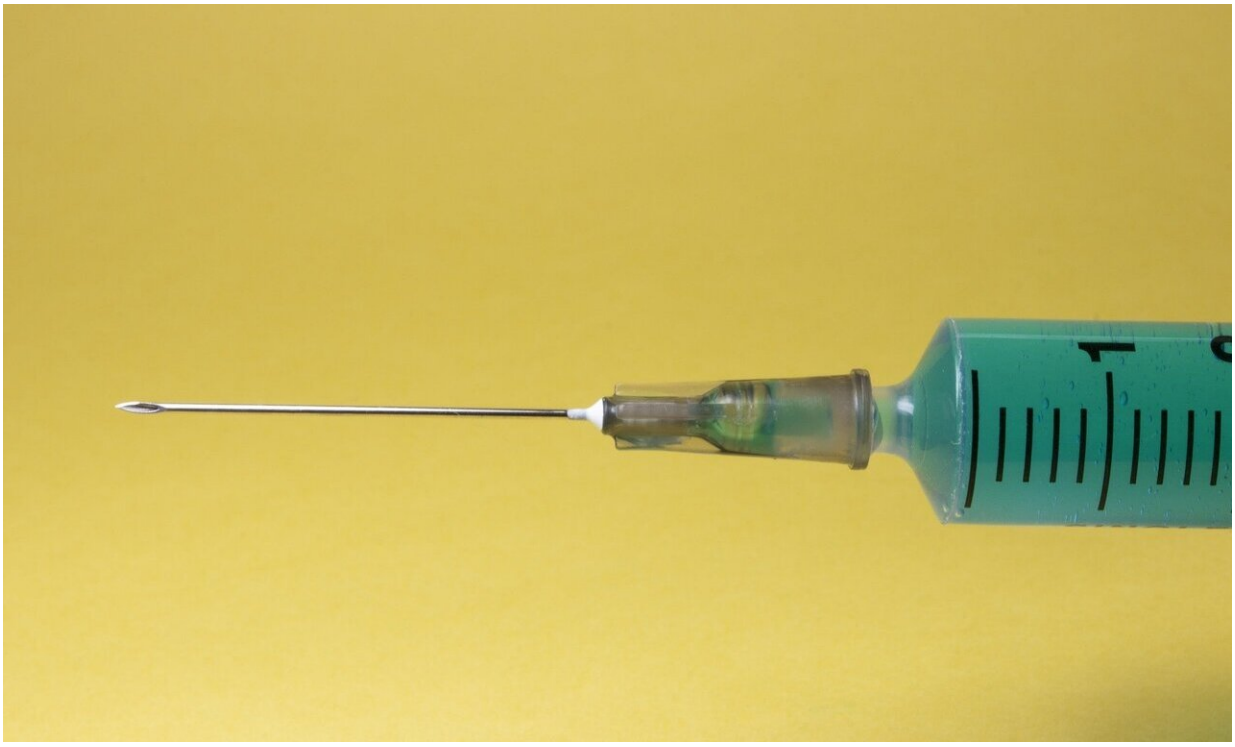

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A subtype of CD8 T cells, which are classically known to promote immune system responses, may be in fact regulating the immune system by suppressing immune cells causing self-destructive responses leading

to autoimmune disorders and organ graft rejection. A team led by researchers from the Department of Medicine and the Transplant Research Center at Brigham and Women's Hospital, in collaboration with researchers from the Dana-Farber Cancer Institute, has developed a vaccine in preclinical models to promote immune regulation.

The work is published in the *Journal of Clinical Investigation*.

The vaccine utilizes synthetically modified natural peptides to stimulate CD8 T regulatory cells. Using a mouse model, the researchers discovered that those self-peptides, presented by a specific class of major histocompatibility complexes, flag harmful immune cells for the body's own regulatory CD8 Tregs to attack and eliminate. The vaccine stimulated and promoted those regulatory T cells that in turn kept the harmful cells under check.

These cells are crucial for maintaining immune responses and preventing inflammation. The researchers found that the developed vaccine prolongs allograft survival in mice and tested anti-allograft immunity on mismatched kidney transplants. An analogous pathway in humans was also identified, implying that this research could protect those with autoimmune disorders or organ transplant patients.

"This new vaccine promotes immune regulation that treats autoimmunity and prolongs kidney allograft survival in mice. Our research identifies an analogous pathway in humans that we hope to target soon," said co-corresponding author Jamil R. Azzi, MD, Ph.D., of the Brigham's Transplant Research Center. "Identification of human T cell receptors homologous to the mouse model tested may form the basis of a novel and effective treatment for disorders that reflect excessive or dysregulated immune responses."

This work was done in collaboration with co-corresponding author

Harvey Cantor MD, of the Dana-Farber Cancer Institute.

More information: Hye-Jung Kim et al, A narrow T cell receptor repertoire instructs thymic differentiation of MHC class Ib-restricted CD8+ regulatory T-cells, *Journal of Clinical Investigation* (2023). DOI: 10.1172/JCI170512