Bone marrow transplantation, using adult stem cells, has been used and studied for decades, because it can potentially provide cures for a variety of diseases. Yet in order to successfully transplant blood stem cells, the patient’s own stem cells must be killed, using chemotherapy or radiotherapy. A mix of cells that includes blood stem cells and immune cells from the donor then attack the tissue of the transplant recipient. This immune attack results in what is called graft-versus-host disease, which can damage tissues and even kill patients.

Since the treatment can be so toxic, it’s only used in critical cases.

Perhaps that is on the road to being solved. Researchers at Stanford have found a way to dramatically lower bone marrow transplant toxicity in mice [2]. If the therapy applies to humans, it could mean cures for autoimmune diseases like lupus and multiple sclerosis, safer organ transplants, and even cures for cancers - without damage to organs.

To do so without chemotherapy or radiotherapy, the scientists sent biology to the rescue.

They started with an antibody against a cell surface protein called c-kit, which is a primary marker of blood stem cells. Attaching the antibody to c-kit resulted in depletion of blood stem cells in immune-deficient mice. “However, this antibody alone would not be effective in immune-competent recipients, who represent a majority of potential bone marrow transplant recipients,” said Stanford research associate Akanksha Chhabra, PhD, in their statement [3]. So they combined it with antibodies and agents that block the CD47 cell surface protein. Blocking CD47 liberated macrophages to “eat” target cells covered with c-kit antibody, Chhabra said.

Once the CD47 marker was blocked and the antibody was attached to c-kit proteins, the immune system effectively depleted the animals’ blood-forming stem cells, clearing the way for transplanted blood stem cells from a donor to take hold in the bone marrow and generate a whole new blood and immune system. After that, a patient’s blood and immune system can safely be replaced, so any disease caused by the patient’s own blood and immune cells could potentially be cured by a one-time application of blood stem cell transplantation, the authors say. Safely
replacing a patient’s blood and immune cells will get rid of the cells that attack their own tissues and produce disease like rheumatoid arthritis and Type 1 diabetes.

This success in mice raises hopes that similar techniques will succeed in human patients. “If it works in humans like it did in mice, we would expect that the risk of death from blood stem cell transplant would drop from 20 percent to effectively zero,” said Judith Shizuru, MD, PhD, professor of medicine at Stanford.

Citation: Akanksha Chhabra, Aaron M. Ring, Kipp Weiskopf, Peter John Schnorr, Sydney Gordon, Alan C. Le, Hye-Sook Kwon, Nan Guo Ring, Jens Volkmer, Po Yi Ho, Serena Tseng, Irving L. Weissman, Judith A. Shizuru, ‘Hematopoietic stem cell transplantation in immunocompetent hosts without radiation or chemotherapy’, Science Translational Medicine, 10 Aug 2016 DOI: 10.1126/scitranslmed.aae0501 [2]