Researchers remove the need for anti-rejection drugs in transplant recipients

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For decades, immunologists have been trying to train the transplant recipient's immune system to accept transplanted cells and organs without the long-term use of anti-rejection drugs. New University of Minnesota preclinical research shows that this is now possible.

In a study published in *Nature Communications*, researchers at the University of Minnesota Medical School's Department of Surgery and Schulze Diabetes Institute, collaborating with colleagues at Northwestern University, have maintained long-term survival and function of pancreatic islet transplants despite complete discontinuation of all anti-rejection drugs on day 21 after the transplant. This study was performed in a stringent preclinical transplant setting in nonhuman primates, one step away from humans.

For many patients with end-stage organ failure, transplantation is the only effective and remaining treatment option. To prevent transplant rejection, recipients must take medications long-term that suppress the body's immune system. These immunosuppressive drugs are effective at preventing rejection over the short term; however, because anti-rejection drugs suppress all of the immune system nonspecifically, people taking these drugs face the risk of serious infections and even cancer. Additionally, non-immunological side effects of immunosuppression, such as hypertension, kidney toxicity, diarrhea, and diabetes diminish the benefits of transplantation. Finally, immunosuppressive drugs are much less effective at preventing transplant rejection over a long period of time, thereby leading to graft loss in many recipients.

Because a growing population of chronically immunosuppressed transplant recipients face that impasse, which might adversely affect their survival, generations of immunologists have pursued immune tolerance as the primary goal in the field of transplantation medicine. Inducing tolerance to transplants would eliminate the need for chronic immunosuppression and enhance transplant and patient survival. Proof that immune tolerance of transplants can be achieved was first demonstrated in mice by Peter Medawar in his Nobel Prize-winning Nature article more than 65 years ago. Yet, despite its immense significance, transplant tolerance has been achieved in only a very few patients.

This new study capitalizes on the unique attributes of modified donor white blood cells, which were infused into transplant recipients one week before and one day after the transplant, thereby recapitulating nature's formula for maintaining the body's tolerance of its own tissues and organs. Without the need for long-term antirejection drugs, islet cell transplants could become the treatment option of choice, and possibly a cure, for many people burdened by type 1 diabetes.

"Our study is the first that reliably and safely induces lasting immune tolerance of transplants in nonhuman primates," said senior author Bernhard Hering, MD, Professor and Vice Chair of Translational Medicine in the Department of Surgery at the University of Minnesota, who also holds the Jeffrey Dobbs and David Sutherland, MD, Ph.D., Chair in Diabetes Research. "The consistency with which we were able to induce and maintain tolerance to transplants in nonhuman primates makes us very hopeful that our findings can be confirmed for the benefit of patients in planned clinical trials in pancreatic islet and living-donor kidney transplantation—it would open an entirely new era in transplantation medicine."

Provided by University of Minnesota