Wafer-thin device has potential to transform the field of islet cell transplantation

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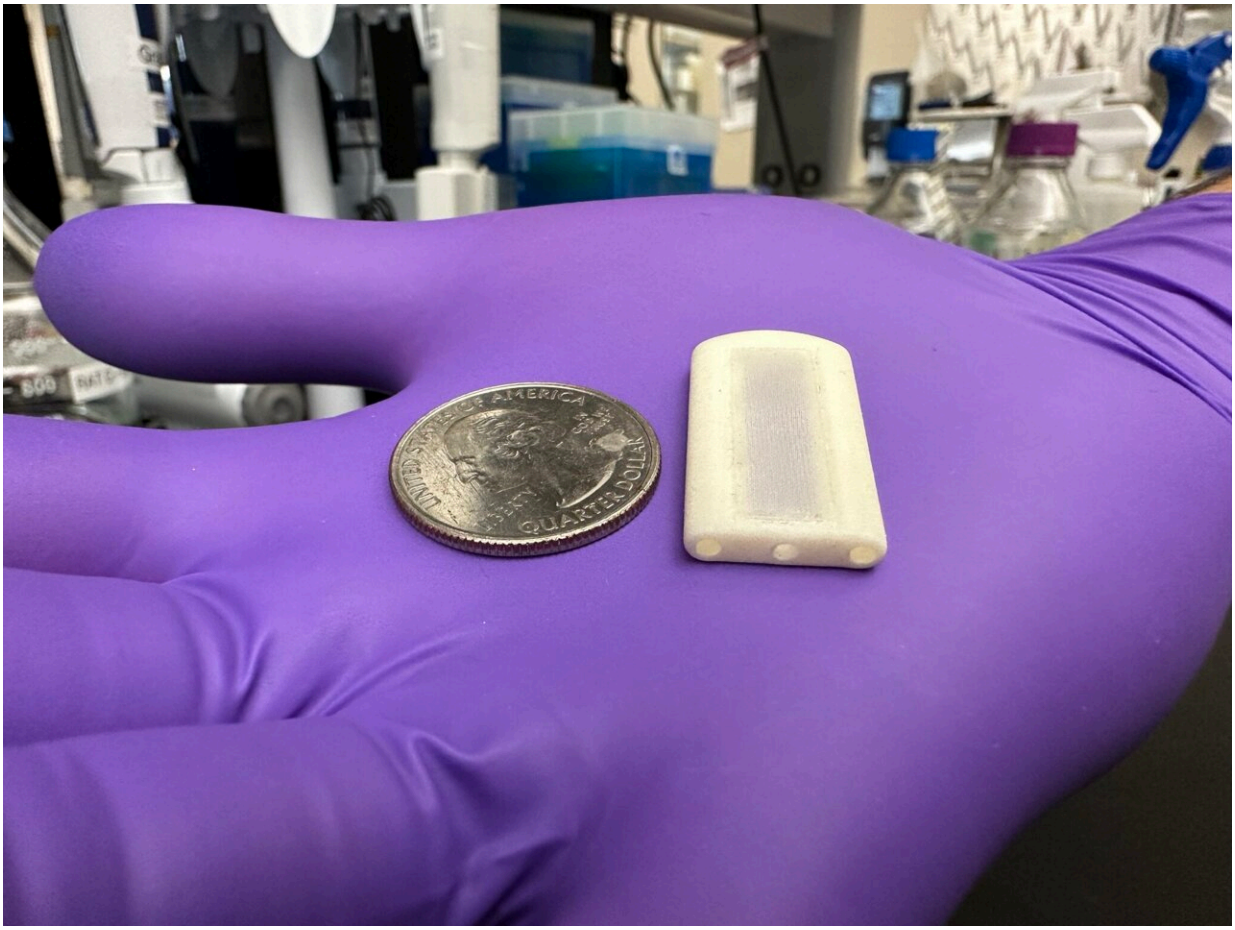

The Neovascularized Implantable Cell Homing and Encapsulation (NICHE) device is about the size of a quarter. Credit: Houston Methodist

A quarter-sized device created at Houston Methodist could drastically alter the course of treatment for type 1 diabetes, a chronic condition that impacts millions of Americans and does not have a cure.

In a study published in the Dec. 26 issue of *Nature Communications*, a research team led by Houston Methodist delivered islet cells and immunotherapy directly into a 3D printed device akin to a bioengineered pancreas, called the NICHE. The treatment restored healthy glucose levels and eliminated type 1 diabetes symptoms in animal models for more than 150 days while avoiding severe adverse effects of anti-rejection therapy by administering immunosuppressive drugs only where the transplanted islet cells were located.

Type 1 diabetes is caused by an autoimmune reaction that destroys the cells in the pancreas that make insulin. It can also cause kidney failure. Daily insulin injections are the most conventional treatment but attaining tight control of glucose levels remains challenging and cumbersome for patients. Further, in more severe cases, patients may need pancreas and kidney transplants, or they may qualify for an islet cell transplant, where the islet cells of a deceased pancreas donor are harvested, processed and then transplanted into the type 1 diabetes patient's liver.

These transplants can help improve a patient's symptoms; however, as with all organ transplants, one of the biggest challenges is the need for immunosuppressive drugs for the rest of their lives to avoid transplant rejection. Lifelong immunosuppression can lead to patients being vulnerable to infectious diseases and increases the risk of certain types of cancer.

The NICHE, created in the Department of Nanomedicine at Houston Methodist Research Institute, is a flat device placed under the skin comprised of a cell reservoir for the islets and a surrounding drug reservoir for localized immunosuppression therapy. It is the first

platform to combine direct vascularization and local immunosuppression into a single, implantable device for allogeneic islet transplantation and long-term type 1 diabetes management. Direct vascularization is fundamental for supplying nutrients and oxygen for maintaining the viability of transplanted islet cells.

"A key result of our research is that local immunosuppression for cell transplantation is effective," said Alessandro Grattoni, Ph.D., corresponding author and chair of the Department of Nanomedicine at Houston Methodist Research Institute. "This device could change the paradigm of how patients are managed and can have massive impact on treatment efficacy and improvement of patients' quality of life."

The NICHE incorporates ports for the refilling of drugs as needed. The researchers refilled the drug reservoirs every 28 days, which is comparable to other long-acting drugs clinically available for migraine prevention or HIV treatment.

Grattoni's team is working on scaling up the NICHE technology for clinical deployment, for which drug refilling may only be needed once every six months. The ability to refill the NICHE technology allows for long-term use in patients. Further, changes in drug formulations or concentration could extend refill intervals to once each year, aligning with routine physician visits.

Grattoni and his collaborators will expand this research over the next few years, with the end goal of testing the NICHE's safety in humans in about three years. Grattoni's nanomedicine lab at Houston Methodist focuses on implantable nanofluidics-based platforms for controlled and long-term drug delivery and cell transplantation to treat chronic diseases.

More information: Jesus Paez-Mayorga et al, Implantable niche with

local immunosuppression for islet allotransplantation achieves type 1 diabetes reversal in rats, *Nature Communications* (2022). DOI: 10.1038/s41467-022-35629-z

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