Biomaterial improves islet transplants for treatment of type 1 diabetes

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Georgia Tech researcher Andrés García. Credit: Georgia Tech

Islet cell transplants are a promising treatment that can cure difficult-to-treat type 1 diabetes. The cells, taken from a donor pancreas, provide patients with a sustainable and tightly controlled source of insulin. A

major problem is getting the patient's immune system to accept the influx of new donor cells; the patient's protective T-cells naturally want to reject the foreign invaders.

But a team of investigators co-led by Georgia Institute of Technology researcher Andrés García overcame this hurdle in previous small animal studies. Their technique uses synthetic hydrogel particles called microgels. The microgels present a potent immunomodulatory protein called SA-FasL to modulate the body's immune response, allowing the transplanted insulin-producing cells to safely do their job, regulating blood glucose levels, and fighting diabetes.

A new study in the journal *Science Advances* from García and his collaborators moves this hopeful treatment strategy closer to the clinic.

"Immunosuppression is a significant problem for patients, but in our prior work we showed that this biomaterial, this microgel, is a potent immunomodulatory molecule, and can induce permanent acceptance of the new cells," said García, the Petit Chair in Bioengineering and Regents' Professor in the George W. Woodruff School of Mechanical Engineering and executive director of the Petit Institute for Bioengineering and Bioscience.

"But that study was done in mice, and the immune system of a mouse if very different from a human's," García added. "And in the progression toward clinical use, you really need to test this strategy in a large animal model."

Now, they have. García and his fellow researchers from the University of Missouri and Massachusetts General Hospital explain their results in the new paper.

Their study, funded by the Juvenile Diabetes Research Foundation,

demonstrates how co-transplanting islet cells with SA-FasL-microgels reversed diabetic symptoms while overcoming the immune response in nonhuman primates. The researchers without using immunosuppressants, which can have dangerous side effects.

The microgels essentially teach the immune system to accept the graft, interrupting the body's inclination to reject the transplant and circumventing the need for continuous immunosuppression.

"Those immunosuppressive regimens are toxic to the patient, so a major goal in the field has been to develop approaches that will allow you to put in this graft and get it to function without chronic immunosuppression," said García.

Because the biomaterial can be created in a lab and shipped anywhere, the new therapeutic is essentially off-the-shelf. And now that they've proven the strategy works in nonhuman primates, García and his collaborators are confident that patients with type 1 diabetes could have a powerful new treatment option.

García is co-founder of the company that licensed the technology, iTolerance, which is already discussing plans for human clinical trials with the U.S. Food and Drug Administration.

"We are pretty pumped—this is very exciting, and these are hopeful results for people fighting type 1 diabetes," said García, corresponding author and part of a 20-person research team. "This work wouldn't have been possible with this team science approach."

More information: Ji Lei et al, FasL microgels induce immune acceptance of islet allografts in nonhuman primates, *Science Advances* (2022). DOI: 10.1126/sciadv.abm9881.
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