Margy Rockwood
July 6, 2022

# ‘Reconforming’ Transplanted Islet Coatings for More Durable Type 1 Diabetes Treatment

A team of researchers at the University of Miami Miller School of Medicine has developed improvements in a hydrogel coating process that lower barriers to transplantation in preclinical models.

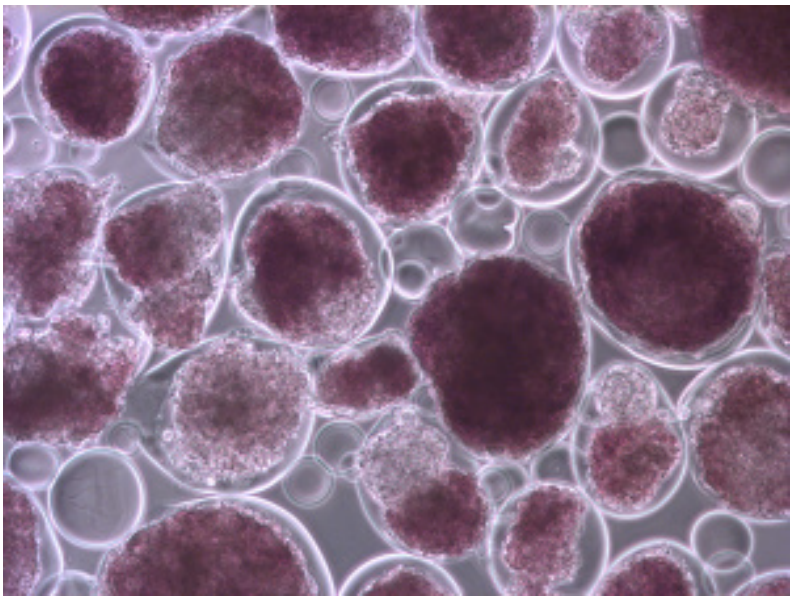
One of the most promising treatments on the horizon for Type 1 diabetes is transplantation of donor islets of Langerhans, the clusters of insulin-producing beta cells that reside in the pancreas. But the viability of this procedure faces some of the same challenges as solid organ transplantations, including autoimmunity, transplant rejection requiring immunosuppression, and poor vascularization.

Dr. Alice Tomei works on encapsulating

islets.

Testing on micro- and macro-encapsulation of the transplanted islets has yielded suboptimal results. Looking for solutions, researchers at the Miller School and the Diabetes Research Institute (DRI), part of UHealth – University of Miami Health System, developed a fluidic method for encapsulating the islets by using a conformal coating with a bioengineered hydrogel. This coating succeeded in providing the needed immune system barrier, while allowing for diffusion of important nutrients and bioactive molecules (such as glucose and insulin) between the transplanted and native tissues.

This process, referred to here as the “direct method,” was superior to prior microencapsulation methods, yet it still had a set of durability, scalability, and other challenges to be overcome.



Coated human islets stained with DTZ

Now the team, led by Alice A. Tomei, Ph.D., associate professor of biomedical engineering at the Miller School and

director of the Islet Immunoengineering Laboratory at the DRI, has completed preliminary testing of an emulsion crosslinking method – an enhanced process for formulating this conformal coating – that addresses these challenges.

## Journal Publishes Findings

In a paper recently published in the journal *Science Advances*, Dr. Tomei, Aaron Stock, Ph.D., a post-doctoral fellow who joined Tomei's lab as a Ph.D. student in 2016, and their colleagues, shared the findings of their preclinical studies.

"Conformal coating microencapsulation technology was an extremely important advancement, enabling us to seriously consider the feasibility of islet transplantation without chronic and systemic immunosuppression. As with every new technology, though, there are wrinkles to be ironed out," Dr. Tomei said. "We were excited to see in our preclinical models that we could largely overcome the major obstacles."

Dr. Aaron Stock holds a tube containing coated islets.

## Addressing Obstacles

The researchers addressed three principal shortfalls of the direct method. One was that the conformal coating process was exposing the cells to be coated to acidic pH levels, which reduced its cytocompatibility. To solve this, they applied a crosslinker-containing emulsion which enabled the gelation to occur after, versus before, encapsulation of the islets, avoiding the toxicity to the islets. This method also allows a fivefold increase in throughput for the several hundred thousand islets that a human transplantation procedure requires.

A second limitation lay in the nature of the peptide viscosity enhancer that was used as additive for the hydrogel coating

solutions. This component is not highly biocompatible and may, in fact, be immunogenic. To address this, the team removed the enhancer and used viscous, minimally crosslinked polymers in combination with the emulsion crosslinking method to adequately enhance viscosity instead.

Finally, the emulsion crosslinking method was able to maintain the thin coating the direct method pioneered (allowing for adequate diffusion of nutrients, etc.), but improved on its viability and biocompatibility to make it durable for long-term implant use.

“In summary,” Dr. Tomei says, “the emulsion crosslinking method preserves the hallmark ‘conformal coatings’ of a covalently cross-linked PEG-based hydrogel on the islet surface, but enhances islet viability, encapsulation yield, and glucose-stimulated insulin secretion.”

Margy Rockwood
July 6, 2022

Drs. Tomei and Stock in the lab

## A Recommendation and Further Study

In the process of testing this method, the team also arrived at a recommendation for where to implant the islets.

“In our lab, the optimal transplant site was the gonadal fat pad versus other sites that have been investigated, such as the subcutaneous (poorer) and intramuscular (poorest) sites,” Dr. Stock explained.

In recent years, pharmaceutical grade hydrogel technology has been leveraged for drug delivery in applications ranging from

optical nerve regeneration to chemotherapy for urothelial cancer.

Because hydrogel consists of a condensed mass of organic polymer enclosing a liquid, and can be semipermeable, it durably encases fluids like drugs or hormones that can be released over time, enables nutrient delivery and oxygenation of a transplanted organ, and also mitigates transplant rejection risks.

## Harnessing ‘Magic’

“We are working on many fronts to bring the magic of hydrogel technology to bear on problems that neither fluids nor solids can solve,” Dr. Tomei said. “The capability of providing immunoisolation to transplanted cells without compromising their secretion of bioactive molecules could be applicable to many areas of regenerative medicine. One is transplantation of allogeneic cells for metabolic function, such as hepatocyte transplantation in liver failure. Another is in stem cell transplantation for patients with spinal cord injury or in renal epithelial cell transplantation, to reduce local inflammation and improve revascularization and regeneration.”

Currently, Dr. Tomei’s team is in active collaboration with Sernova Corp., which licensed Dr. Tomei’s conformal coating technology from the University of Miami, to pave the way for safe and effective islets of Langerhans transplantation.

Drs. Tomei and Stock are hopeful that they are not far from a regenerative medicine therapeutic cure that will not require life-long immunosuppression medications.

Content Type Article