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Researchers Develop Novel Method for Protecting Islets after Transplantation for Type 1 Diabetes

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An international research team led by investigators at the Miller School's Diabetes Research Institute has developed a novel method of protecting diabetes-reversing islets that may prevent islet rejection or destruction by the immune system after they are transplanted in Type 1 diabetic patients.

The conformal coating process — similar to shrink wrapping, but on a microscopic level — offers distinct advantages over traditional encapsulation methods. The results, "Device Design and Materials Optimization of Conformal Coating for Islets of Langerhans," are being published online in the *Proceedings of the National Academy of Sciences.*

"Previous efforts in islet encapsulation have failed partly because of the large size of conventional capsules," said **Alice Tomei, Ph.D.**, assistant professor of surgery at the Diabetes Research Institute (DRI), principal investigator and lead author of the article. "Islets vary considerably in size and shape, and production of traditional capsules is standardized to accommodate the largest size. This results in capsules that are too large for the smaller islets. The extra space inside the capsule delays access to oxygen and nutrients, causing many islets to die. It also delays the islet's main function — sensing blood glucose and releasing the right amount of insulin in real time to avoid hyper- and hypoglycemia."

Tomei and her team set out to develop a new method — one that would coat pancreatic islets with a thin layer of biomaterial to protect them from immune-response attacks, but that would not impact islet size, which can limit the availability of transplantation sites. The process involves running the islets through a polymer jet, giving each one a tight coating in the shape of the islet itself.

The research began several years ago, when Tomei was working at the Institute of Bioengineering at the École Polytechnique Fédérale de Lausanne in Switzerland in the laboratory of **Jeffrey A. Hubbell, Ph.D.**, the article's senior author. She came to the DRI in 2010, bringing the research with her.

The conformal coating method also seeks to overcome a material-quality problem that has plagued traditional encapsulation efforts.

“Poor stability of the capsule material, which is mainly based on alginate, causes a change in the permeability to molecules and cells that are critical for immunoisolation, as well as capsule breakage after implantation,” Tomei said. “This ultimately results in rejection of the enclosed cells.”

By contrast, the material used in the conformal coating is a hydrogel, somewhat like a porous contact lens. It allows food and oxygen to get in, and waste to get out, without any delay in insulin secretion. In addition, because it doesn’t take up the same amount of space as conventional capsules, the conformal coating offers researchers a greater variety of transplantation sites. This includes DRI’s recently introduced BioHub “mini-organ,” a sponge-like silicone wafer that can be filled with islets and implanted to function as a pancreas replacement.

“Pancreatic islets are the most sensitive cells that I have worked with, and keeping them happy while enclosing them in a protective bubble is a very hard task,” said Tomei. “We believe conformal coating represents a breakthrough in the field of islet transplantation.”

Studies of conformal-coated islets in models of islet transplantation for Type 1 diabetes are ongoing in rodents. If they continue to be successful, Tomei estimates that human clinical trials could begin in a few years.

Additional DRI investigators who contributed to the research and the journal article are Christopher Fraker, Ph.D., research assistant professor of surgery and cell transplantation; Jaime Giraldo, Ph.D. candidate; Vita Manzoli, M.S., senior research associate and Ph.D. candidate; R. Damaris Molano, D.V.M., scientist; Mejdi Najjar, B.S., research associate; Antonello Pileggi, M.D., Ph.D., professor of surgery and Director of the Preclinical Cell Processing and Translational Models Program; Camillo Ricordi, M.D., Scientific Director; Cherie L. Stabler, Ph.D., associate professor of biomedical engineering and surgery, and Director of the Tissue Engineering Program; and Diana Velluto, Ph.D., post-doctoral fellow.

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