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Japan invents novel cell therapy for type I diabetes mellitus

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A novel device for the safe and effective transplantation of human-induced pluripotent stem cell (iPSC)-derived pancreatic beta-cells in type I diabetes mellitus

Researchers from The University of Tokyo have developed a novel device for the safe and effective long-term transplantation of human-induced pluripotent stem cell (iPSC)-derived pancreatic beta-cells in type I diabetes mellitus.

T1D develops when autoimmune antibodies destroy pancreatic beta-cells that are responsible for the production of insulin. The current mainstay of treatment for T1D is to inject insulin.

"Treating type I diabetes mellitus by Cell therapy is challenging. It's difficult to make large amounts of human beta-cells in a dish and to achieve safe and effective transplantation. In this study, we wanted to develop a novel construct that enables successful transplantation of beta-cells in the long-term" says the lead author of the study Professor Shoji Takeuchi.

The researchers developed a lotus-root-shaped cell-encapsulated construct (LENCON) and packaged it with human iPSC-derived pancreatic beta-cells, which are a limitless cell source and allow for the production of any number of beta-cells. The necessity for such an encapsulation technique arises from the fact that immune cells of the recipient could destroy the newly transplanted cells. To prevent this from happening, the researchers constructed the LENCON graft with millimeter thickness.

The millimeter-thick graft diameters have previously been shown to mitigate the body's immune response to a foreign body. At millimeter thickness, oxygen and nutrients could not be supplied to the center of the cells, but by using a lotus root shape, the cells were placed only near the edge of the graft where oxygen and nutrients can diffuse sufficiently, creating an environment in which the cells could survive, even in the millimeter-thick graft.

The researchers transplanted the construct in immunodeficient and immunocompetent diabetic mice. The former helped investigate the efficacy of the graft on controlling blood glucose levels in the absence of an immune response, while the latter approach tackled both goals. The researchers found that LENCON was able to maintain normal blood glucose levels for more than 180 days in the former mice, and was able to be removed without adhesion after more than one year of transplantation in the latter mice.

"These are striking results that show how LENCON can successfully and safely be used in the setting of type I diabetes

mellitus. Our results suggest that LENCON could offer a novel option for cell therapy for type I diabetes mellitus," says the first author of the study Dr. Fumisato Ozawa.