BIOENGINEERING OF FUNCTIONAL NEO-ISLETS IN VIVO USING CELL SHEET TECHNOLOGY

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[Introduction] Cell-based therapy using pancreatic islets has been developed as a promising new approach for treating insulin-dependent diabetes mellitus (DM). To advance in the islet-based therapies for DM, further improvements are required to optimize the procedures to maximize the longevity of the transplanted islet cells. In this context, it has been highly expected to create an approach to bioengineer functional islet tissues at sites other than the liver. The present study discusses a novel tissue engineering approach for DM by fabricating a monolayered tissue sheet composed of dissociated single pancreatic islet cells for the creation of functional and neo-islet tissues in vivo.

[MATERIALS AND METHODS] Temperature-responsive culture dishes specific to islet cell culturing were prepared by covalent immobilization of the temperature-responsive polymer poly(N-isopropylacrylamide) (PIPAAm) to the plastic dishes followed by coating with laminin-5 (1, 2). Dissociated pancreatic islet cells were obtained from Lewis rats and were then plated onto the laminin-5-PIPAAm dishes. After the cells reached confluency, cultured islet cells were harvested as a uniformly connected tissue sheet by lowering the culture temperature. The functionality of the harvested islet cell sheet was examined by histological examination, cell culture conditions, and functional activity following transplantation into diabetic individuals.

[RESULTS] Histological examination showed that the harvested cell sheet had a monolayered 2-D structure. Immunohistological staining revealed that the islet cell sheet predominantly comprised of insulin- (76%) and glucagon- (22%) staining positive cells, respectively. Upon re-plating of the islet cell sheet onto new culture dishes, we detected a positive response of the islet cell sheet to a glucose-challenge test. By transplanting the islet cell sheets into the subcutaneous space of SCID mice, islet tissues were successfully engineered and sustained. Therapeutic effectiveness of this islet bioengineering procedure was confirmed in the transplantation study to the Streptozotocin-induced diabetic SCID mice.

[CONCLUSIONS] The present study describes a new proof-of-concept approach to generate monolayered functional neo-islets in vitro. Furthermore, therapeutic value for the DM of the islet tissue engineering approach using the islet cell sheet was experimentally confirmed in the present study.

References

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