A bio-inspired hybrid nanosack for pancreatic islet transplantation in the omentum

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Statement of Purpose

Pancreatic islet transplantation has demonstrated consistent and sustained reversal of type 1 diabetes, generating optimism for its wider application as a potential cure for type 1 diabetes. The omentum is an attractive site for pancreatic islet transplantation as it allows a large implantation volume, ease of surgical manipulation, and some immune privileges. However, revascularization is one of major challenges in the omentum due to its low vascularity. Fibroblast growth factor-2 (FGF-2) is known to stimulate angiogenesis, and its controlled release in the omentum could enhance islet revascularization. The goal of this study is to develop an innovative strategy to increase the efficacy of pancreatic islet transplantation in the omentum using the bio-inspired hybrid nanosack. The hybrid nanosack was created with a combination of **1)** a self-assembled peptide amphiphile (PA) nanomatrix gel capable of encapsulating islets with a nurturing microenvironment[1] and **2)** a poly (ε-caprolactone) electrospun (ePCL) nanofiber sheet with porous crater-like structures for infiltration of blood vessels and a mechanically stable protective structure for surgical manipulation. The hybrid nanosack also provides a highly controlled delivery of FGF-2 for islet revascularization in the omentum. Outcomes from this study will support the feasibility of the hybrid nanosack for enhanced islet engraftments in the omentum.

Research Design and Methods

Crater like structures on the ePCL nanofiber sheet were fabricated by gas foaming/salt leaching technique and characterized by scanning electron microscopy (SEM) and 3-D confocal microscopy. *In vitro* human umbilical vein endothelial cell (HUVEC) infiltration test through the ePCL nanofiber sheet was performed. To create the hybrid nanosack, FGF-2 was encapsulated within the PA nanomatrix gel and wrapped within the e-PCL nanofiber sheet with crater like structures coated with FGF-2. Release kinetics of FGF-2 from the hybrid nanosack (enzyme-linked immunosorbent assay, ELISA) was studied. FGF-2 activity test was performed by HUVEC proliferation using MTS assay. To evaluate an angiogenesis at the omentum site, the hybrid nanosack was implanted within the rat omentum. Two weeks after implantation, angiogenesis was evaluated using micro-CT analysis.

Results

The porous crater-like structures were successfully created with pore sizes of approximately 200-400 μm in diameter (Figure 1).

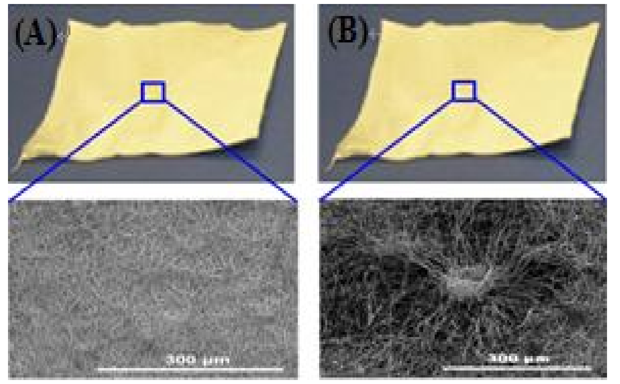

Fig. 1. (A) Traditional e-PCL nanofiber sheet and SEM image. (B) e-PCL nanofiber sheet with crater like structures and SEM image.

These porous crater-like structures allowed HUVEC infiltration through the e-PCL nanofiber sheet. The hybrid nanosack also showed multi-stage FGF-2 release kinetics. We evaluated the hybrid nanosack stimulation of neovascularization using Micro-CT analysis. Figure 2. shows that angiogenesis occurred surrounding the hybrid nanosack in the omentum. Arrows in b) indicate micro-blood vessels invaded the hybrid nanosack and purple vessels in c) also demonstrate that high density vasculatures were generated within the hybrid nanosack.

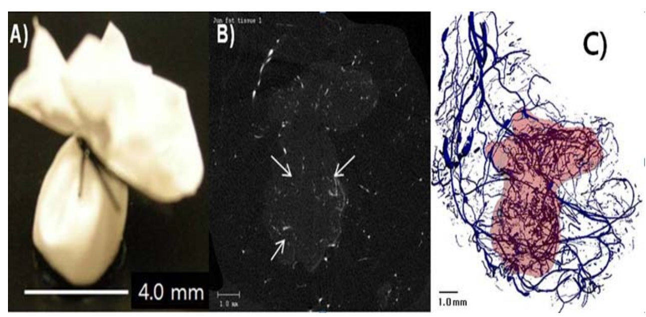

Fig. 2. (A) Hybrid nanosack (B) acquired sectioned 2D and (C) 3D μ-CT images of implanted hybrid nanosack in the omentum of a rat after 2 weeks.

Conclusion

We have successfully developed the hybrid nanosack which enhanced revascularization at the omentum site of rat. Therefore, these novel strategies have great potential to promote islet survival, engraftment, and stable long term function at the omentum site.

Reference: 1. Lim. D. J. Tissue Eng. 2011. 17 (3-4): 399-406.

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