INTEGRATION OF PANCREATIC AGGREGATES INTO A BIOSILK NETWORK TO TREAT DIABETES

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Diabetes type 1 is a life-threatening disease that accompanies a life-long insulin dependency and limits the quality of life. An efficient way to treat diabetes is pancreatic islet transplantation. However, pancreatic islet transplantation has major disadvantages, e.g., massive loss of islets and donor shortage. These problems could be solved by using insulin-producing pancreatic aggregates differentiated human pluripotent stem cells (hPSCs) combined with a biomaterial based on unique 3D spider silk (BioSilk) scaffold to protect pancreatic aggregates during the transplantation. BioSilk is recombinantly produced in *E.coli* and is functionalized with a fibronectin motif to promote cell adhesion. Incorporated pancreatic aggregates in BioSilk networks may be used as a novel cell therapy to treat diabetes type 1.

This study aims to develop an optimal protocol for the incorporation of pancreatic aggregates. We have analyzed the viability and oxygenation of pancreatic aggregates incorporated in BioSilk networks derived from human embryonic stem cells at different time points during a cultivation period of 3 weeks. Furthermore, we compared the functionality of free-floating pancreatic aggregates to incorporated ones by measuring the expression of c-peptide (insulin) and glucagon expressing cells using flow cytometry, quantitative PCR, and immunohistochemical staining. Specifically, the transcriptome was analyzed on a single cell level to compare the gene expression profile and heterogeneity of free-floating pancreatic aggregates and incorporated pancreatic aggregates.

We have demonstrated a reproducible and simple method for the integration of pancreatic aggregates. This method leads to a stable 3D network with a good distribution of pancreatic aggregates. High viability and oxygen level were proven by pancreatic aggregates incorporated in BioSilk networks over the cultivation period. Functionality was maintained during cultivation within BioSilk networks with related insulin and glucagon expression in free-floating pancreatic aggregates to incorporated pancreatic aggregates. It could even be shown that BioSilk enhances pancreatic islet function by increasing insulin expression. In conclusion, BioSilk serves as an excellent biomaterial to incorporate pancreatic aggregates for transplantation to diabetic patients.