Enhancement of Pancreatic Islet Cell Viability via a 3D bioengineered Matrix

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Introduction:

Diabetes Mellitus is chronic devastating disease that causes severe complications. Transplanation of insulin producing pancreatic islets of Langerhans is a promising strategy to treat type 1 diabetic patients. However, shortage of islet donors, poor islet survival and toxicity of anti-rejection drugs often reduce the graft functional lifetime. Here, we developed a novel bioengineered crosslinked CM (CCM) to provide optimal matrix biomimetic for islet cell and thus, improve their viability and function.

Methods:

We previously showed that a fibroblast populated-collagen matrix (CM) significantly improved engrafted islet viability/function. However, this composite was prone to gradual biodegradation and contraction. Moreover, to avoid use of systemic anti-rejection drugs, we proposed the use of a local immunosuppressive enzyme, indoleamine-2,3-dioxygenase (IDO). Viability and insulin secretory function of islets embedded within fibroblast populated CCM (FP-CCM) was evaluated *in vitro* and *in vivo*. IDO expression was transduced in fibroblasts by a lentiviral vector carrying IDO gene and islet viability was evaluated in the presence and absence of IDO producing cells.

Results:

Islet survival/function markedly improved within fibroblasts populated Crosslinked collagen matrix (FP-CCM). The results showed that local lentiviral induction of IDO delivered by fibroblasts is nontoxic to the embedded islets and can suppress immune responses against islets. FP-CCM evidently preserved normal morphology and insulin/glucagon production in grafted islets. FP-CCM also preserved islet insulin secretory function and reduced fibroblast proliferation rate.

Discussion:

The findings of the present study clearly show that the novel CCM when populated with fibroblasts not only has the beneficial properties of the collagen scaffolds but also addresses two major concerns with FPCM that are poor biomimetic and gradual disintegration. This promising finding offers a new approach to improving islet transplant outcome.