Tissue-engineered platform for cell replacement and immunomodulation in autoimmune diabetes

Autoimmune destruction of insulin-secreting beta cells in pancreatic islets leads to type-1 diabetes. Type-1 diabetes affects millions of people worldwide and requires blood glucose monitoring and exogenous insulin injections. Currently, there is no treatment to block beta cells destruction and prevent type-1 diabetes. Islet transplantation may cure type 1 diabetes but this procedure is currently limited by the need for lifelong chronic immunosuppression. We are developing tissue engineering platforms to block beta cell destruction before disease onset and for improving beta cell transplantation in established type-1 diabetes. Our platform integrates immunomodulatory biomaterials with cells that can dampen immune responses against beta cells and with cells that secrete insulin to regulate blood glucose. One platform (*Fig. 1)* exploits immunoisolating hydrogels for encapsulation of insulin-secreting cell clusters, which may allow cell transplantation without immunosuppression. We developed an encapsulation technology that allows 'wrapping' each individual cluster with a uniformly thin hydrogel layer. By reducing the diffusion distance 10-fold over traditional encapsulation technology, this conformal coating encapsulation maximizes nutrient transport. Another tissue-engineered platform we have developed in the lab (*Fig. 2)* allows exploiting the function of immunomodulatory hydrogel and of stromal cell networks in dampening the immune cells that attack beta cells. We found that a particular subpopulation of stromal cells in lymph nodes is affected in type-1 diabetes. We have developed collagen scaffolds that allows recreating stromal cell three-dimensional reticula that mimics the cell organization in lymph nodes. We will use our engineered stromal cell reticula for mechanistic studies and for transplantation therapy in type-1 diabetes. We are currently testing our tissue-engineered platforms for cell replacement and for immunomodulation in preclinical models of type-1 diabetes. This work is needed before we can test our platforms in humans.

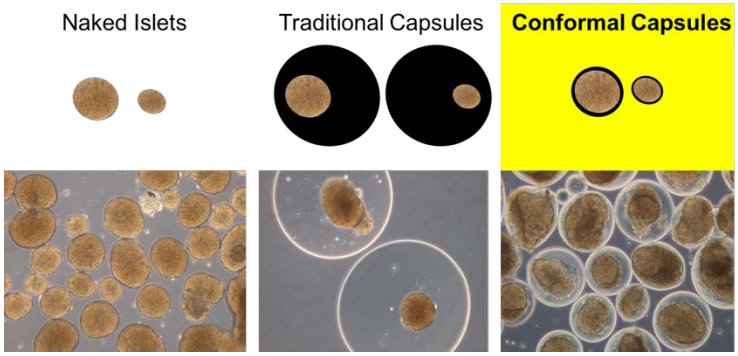

Fig. 1. Tissue-engineered platform for transplantation of pancreatic islets without immunosuppression in type-1 diabetes.

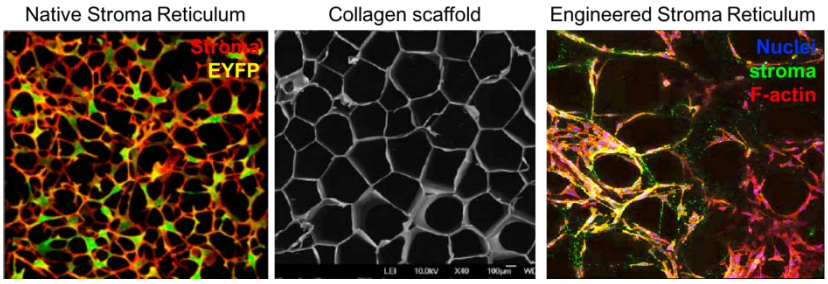

Fig. 2. Tissue-engineered platform for exploiting the immunomodulatory properties of stromal cell reticula in type-1 diabetes.