

# TISSUE ENGINEERING STRATEGIES FOR DIABETES TYPE I TREATMENT

## MICROWELL BASED SCAFFOLDS FOR TRANSPLANTATION OF ISLETS OF LANGERHANS IN TYPE I DIABETES

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Diabetes type I is an autoimmune diseases, in which patients suffer from self-destruction of beta cells residing in the islets of Langerhans located in the pancreas. As a results these patient suffer from hyperglycemia, which ultimately can lead to symptoms such as retinopathy, heart and kidney failure as well as atherosclerosis. Currently, there are several therapies available to manage blood glucose levels, like regular insulin injections or automated insulin pumps. Another possible therapy is the infusion of allogeneic Islets of Langerhans isolated from donor pancreata according to the so-called Edmonton protocol<sup>1</sup> into the portal vein. Approximately 80% of the transplanted islets die within a few days after transplantation. To improve islets survival we are exploring the use of scaffolds as an alternative for infusion in the portal vein. We use hot and cold embossing techniques to create micro well patterned films based on PEGT-PBT block copolymers to create a proper microenvironment for Islets aggregation and retainment. Cytotoxicity tests proved that the scaffolds were non toxic and comparable to micro wells created from poly-lactic acid which was used as a control. The micro well scaffolds with diameters of ~130µm and ~330µm were treated with and without argon plasma treatment to study cell adherence after seeding. The thin films with microwell scaffolds (50-100 µm) did not allow glucose diffusion, which is probably due to the slight hydrophobic nature of these carriers. This was confirmed by contact angle measurements. First analysis of the newly fabricated scaffolds with human and murine islets showed that the islets retained their proper morphology and responded to a rise in glucose in the culture medium by secretion of insuline. Plasma treatment had no detectable effect on cell spreading.

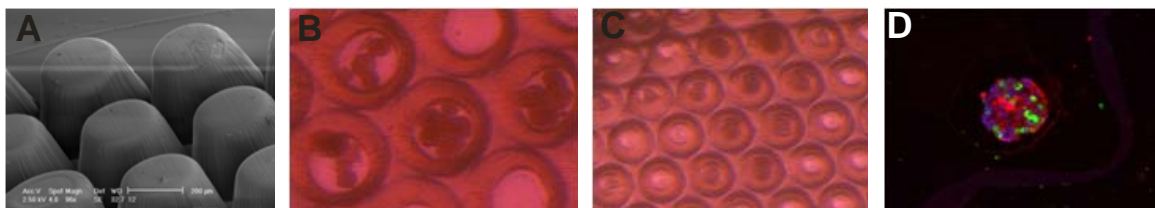


Fig. 1: A: Micro-formed scaffold, B: human islets in 300 µm wells, C: human islets in 130 µm wells, D: crosssection of a single human islet in 130 µm well stained for DNA (blue), insulin(red) and glucagon (green).

We conclude that transplantation of islets of Langerhans in a microwell based scaffold might provide an alternative future therapy for Islets transplantation in Diabetes type I patients.

1) Shapiro AMJ, Lakey JRT, Ryan EA, Korbitt GS, Toth E, Warnock GL, Kneteman NM, Rajotte RV. Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. N Engl J Med. 2000;343:230-238.