T3: TEXAS A&M TRIADS FOR TRANSFORMATION
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Vascular Islet-on-a-chip biosystem

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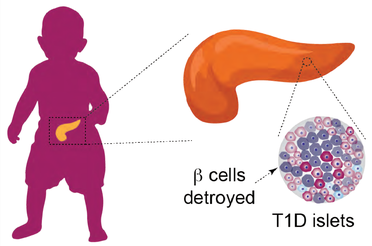
Motivation



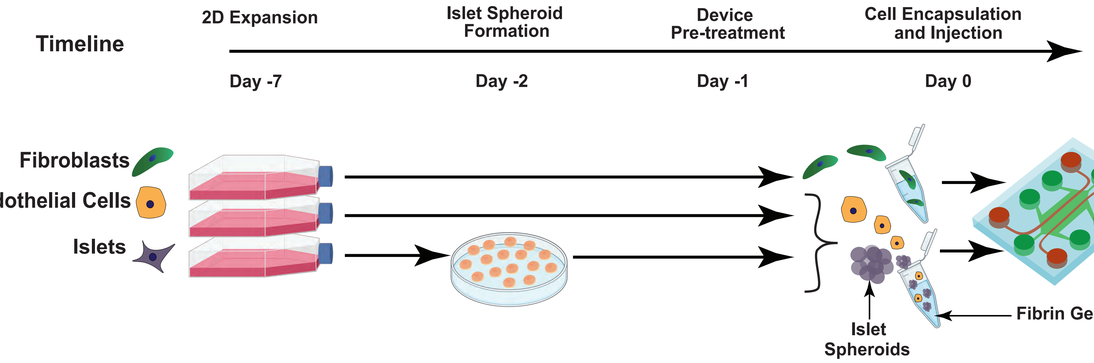
Pancreatic islet transplantation is a tissue engineering approach to regenerating glucose-stimulated insulin response to patients suffering from Type I Diabetes (T1D).

However, islet grafts (and tissue engineering in general) still lack microvascular networks that support an implant's viability via nutrient and was transportation.

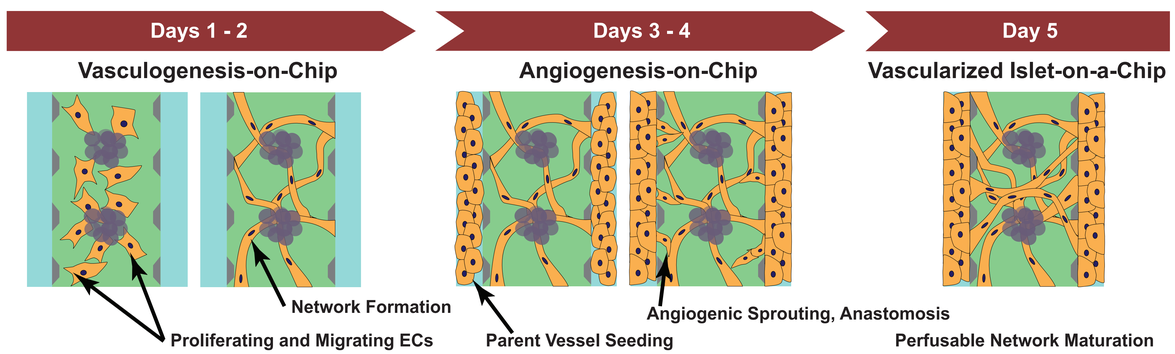
Here, we have developed a vascularized islet biosystem featuring tunable biomaterials that optimize islet health and microvascular network formation

Biosystem Fabrication

Biosystem Pre-Culture



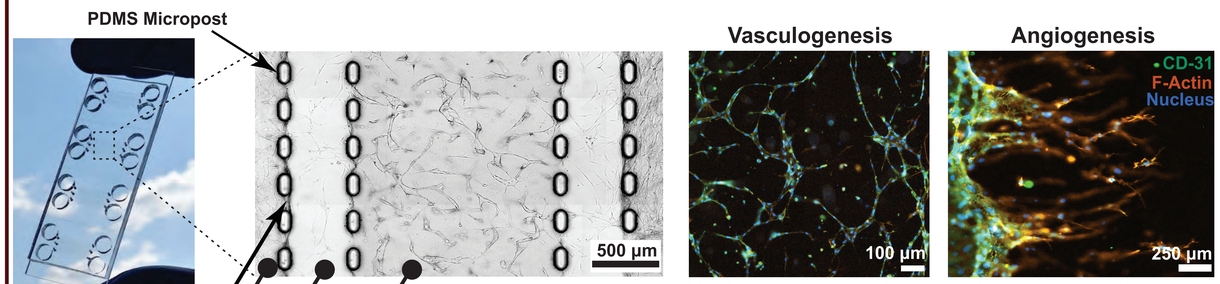
Biosystem Self-Assembly



First, individual endothelial cells migrate and proliferate, forming islands of tubular networks. However, these networks create a closed system, where the islets and newly formed vascular network remain closed off from the fluidic channels of the biosystem. Nutrient and waste transportation thus rely on simple diffusion of solutes through the biomaterial scaffold.

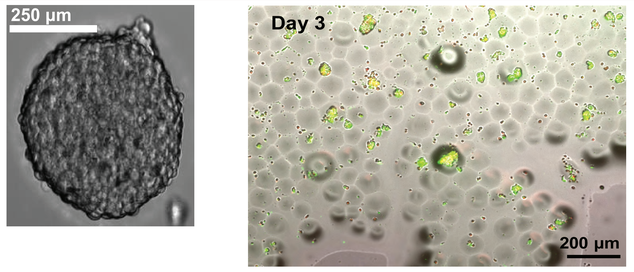
Parent vessels are seeded adjacent to the central channel and anastamose with the main microvascular network via angiogenesis by day 3. Following tube maturation, a functional, perfusable microvascular network supports islets on-chip, therefore providing a testing bed for studies on T1D pathogenesis, pharmacological intervention, as well as tissue engineering strategies for optimizing immunoprotection and vascularization of islet grafts.

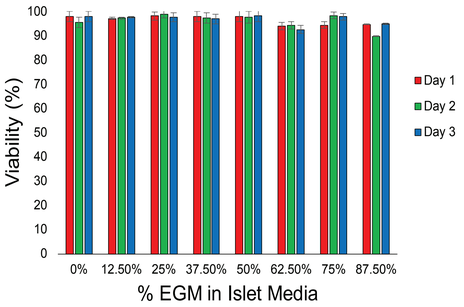
Self-Assembled Microvascular Networks



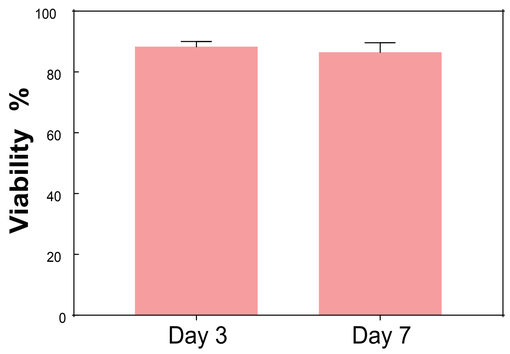
A standard microscope slide contains four biosystems, each of which consist of five compartments separated by PDMS microposts. Here, fluid-hydrogel interfaces form that allow cell encpasulation, solute diffusion, and cell migration.

Islet Encapsulation and Co-culture with ECs





Islet Viability following PEG Encpasulation



Microfluidic methods such as hanging drop microchannels and T-junction channels were used to form islet spheroids or encapsulate single Beta Cells.

Microvascular network formation relies on EC-specific cell culture medium. Islet spheroids remained viable after long-term culturing in EC media.

Spheroids were tested in different biomaterials such as fibrin and PEG hydrogel. Long-term viability was maintained following encpasulation.

Future Directions

1. Glucose-stimulated insulin response.
2. Biomaterial tuning for vascularization optimization.
3. T1D induction via streptozocin treatment or trained immune cells.

Acknowledgements

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