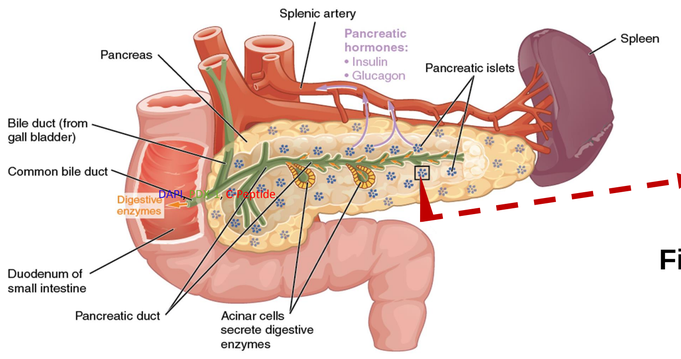
# Islet on a Chip – Engineering a Biomimetic Microsystem for Human Pancreatic Islets

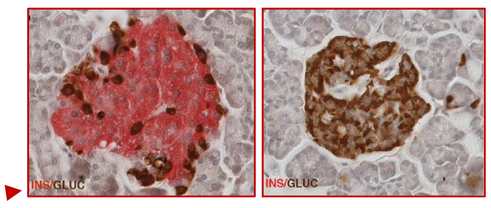
Alanna R. Gannon[1,2], Benjamin D. Pope[1,2,3], Aaron L. Glieberman[1,2], Kevin L. Shores[1,2], Quinn P. Peterson[3], Douglas A. Melton[3] and Kevin K. Parker[1,2]

1. Disease Biophysics Group, John A. Paulson School of Engineering and Applied Sciences, Harvard University, 2. Wyss Institute for Biologically Inspired Engineering at Harvard University, 3. Harvard Department of Stem Cell and Regenerative Biology

## Background

- **The Problem: Type I diabetes is an autoimmune disease in which the insulin producing beta cells in the islets of Langerhans are selectively destroyed by auto-reactive T-cells.**
- **For unclear reasons, the rate of T1D in children is rising by 3% annually**

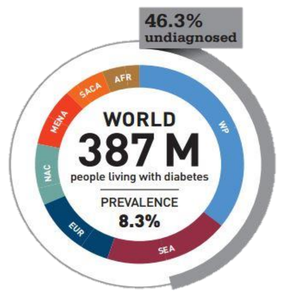



Healthy Islets Diseased Islets

**Figure 1 | Islets stained for insulin (red) and glucagon (brown)**

- **Hypothesis: Recapitulating the mechanical and chemical micro-environment of native pancreatic islets in a microfluidic device will enable evaluation of insulin release sensitivity, calcium flux and long term survival of beta cell populations**
- **Providing an in vitro specialized model that permits simulation, mechanistic investigation and pharmacological modulation of pancreatic islets**




International Diabetes Federation

## Main Achievements

**Chip Housing Design:**

- **We have designed and fabricated a polymeric microfluidic device capable of housing encapsulated SC-beta cell clusters.**
- **Within the polymeric chip, the cell clusters are held in wells of a circular cartridge disk, thermally bonded to a porous polycarbonate membrane (Figure 2).**
- **These wells are cut into the cartridge using UV laser patterning creating a radial design which enables flow from the upper central channel to spread radially outwards on the cartridge thus ensuring a uniform distribution of fluid shear over the encapsulated islets.**

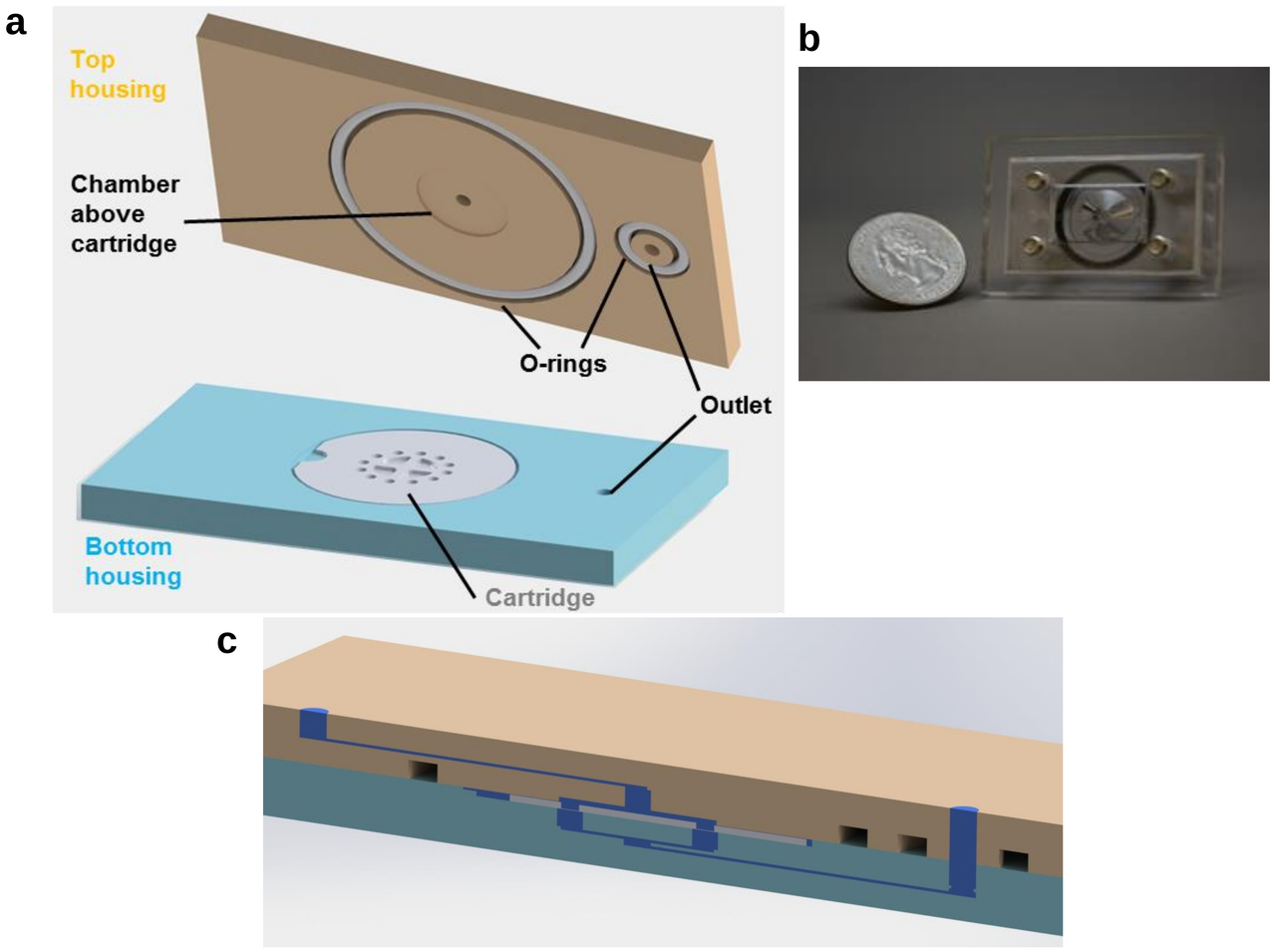



**Figure 2 | Islet Chip Development. a. Brown components combine to form the top of the device. Blue components form the bottom. Gray is the cartridge which houses the cells, and is sandwiched between top and bottom. b. An image of the fabricated chip. c. A section of the chip highlighting the fluid chamber within the chip.**

## Main Achievements

- **In order to determine oxygen and glucose kinetics through our device we have created a mathematical model of our chip design that can indicate potential problem areas for cell hypoxia (Figure 3).**

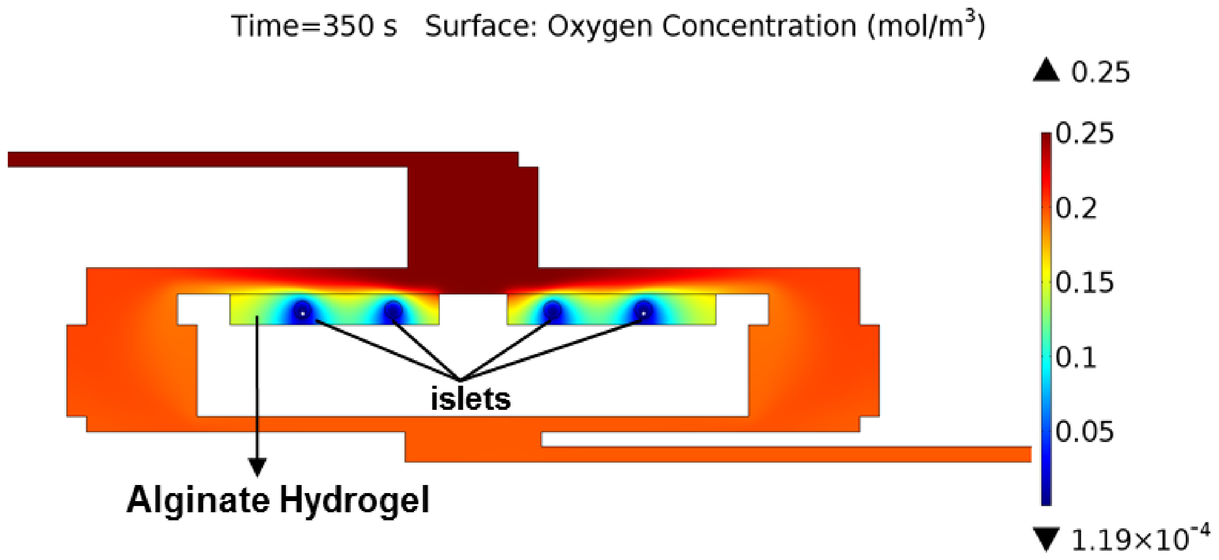



**Figure 3 | 2D COMSOL model of cartridge chip showing $o_2$ transport consumption by islets (left). White areas inside islets indicate possible regions of cell necrosis due to hypoxia ($O_2$ conc. < 0.0001 mol/m$^3$)**

- **Islets, like other tissues, are heavily influenced by cell-ECM interactions.**
- **We therefore sought to determine the functional significance of SC-beta cell and native islet ECM protein interactions, in particular focusing on identity and insulin secretion (Figure 4).**
- **Our initial results suggest incorporation of specific ECM components into our hydrogels will be important for the long-term viability and function of our chip.**

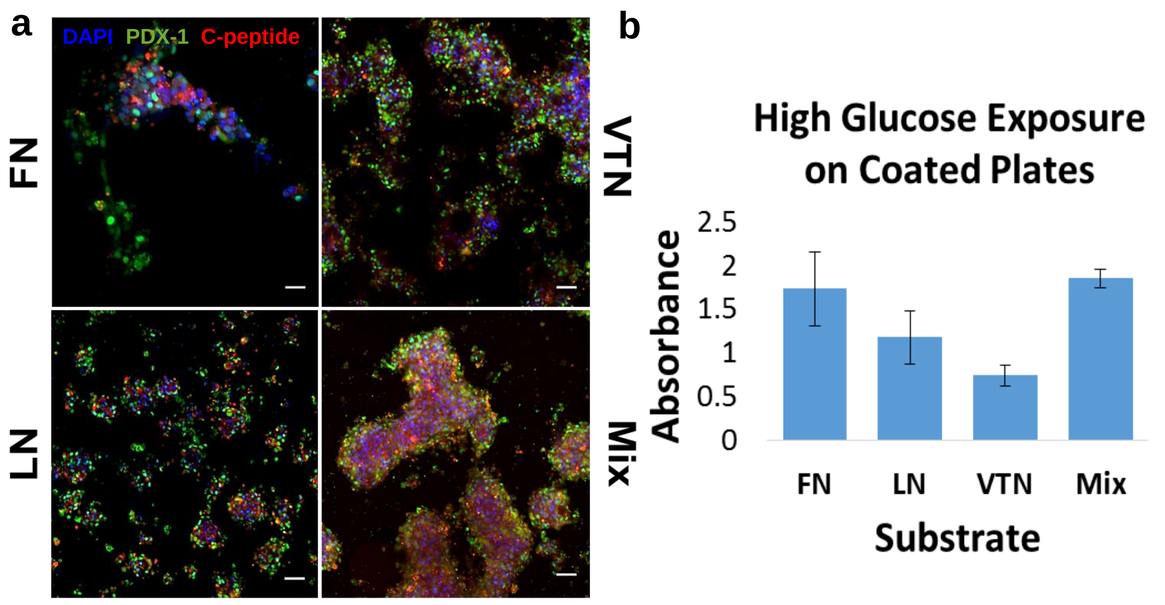



**Figure 4 | a. SC beta cells cultured on islet ECM substrates; fibronectin (FN), laminin (LN), vitronectin (VTN) and a mixture. b. Corresponding absorbance values of cultures were to high glucose stimulation Mag. 10x, scale bar 100 µm.**

- **To aide in this process, we are working in combination with the Melton lab, to further investigate what specific proteins are present in SC derived beta cells during differentiation.**

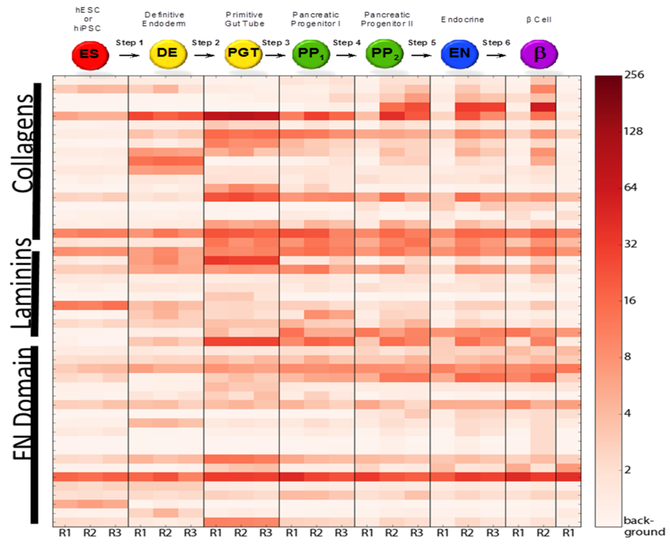



**Figure 5 | Microarray analysis of transcripts during ES to beta cell differentiation.**

## Impact & Future Directions

- **In the future, we will continue to test additional extracellular matrix components in isolation and combination in an effort to enhance *in vitro* culture conditions.**
- **To this end we will encapsulate hES-pancreatic beta cell clusters in hydrogels of varying stiffness and composition that mimic the native islet microenvironment in order to optimize and maintain function of the mature beta cells in long-term culture.**
- **Our islet chip will allow for the development of reproducible disease models, enhance preclinical evaluations of potential diabetic therapeutics and provide clinically relevant readouts of pancreatic beta cell function.**

## Acknowledgements

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