Pancreatic Islet-on-a-Chip

Engineering a Biomimetic Microsystem for Stem Cell Derived Islets

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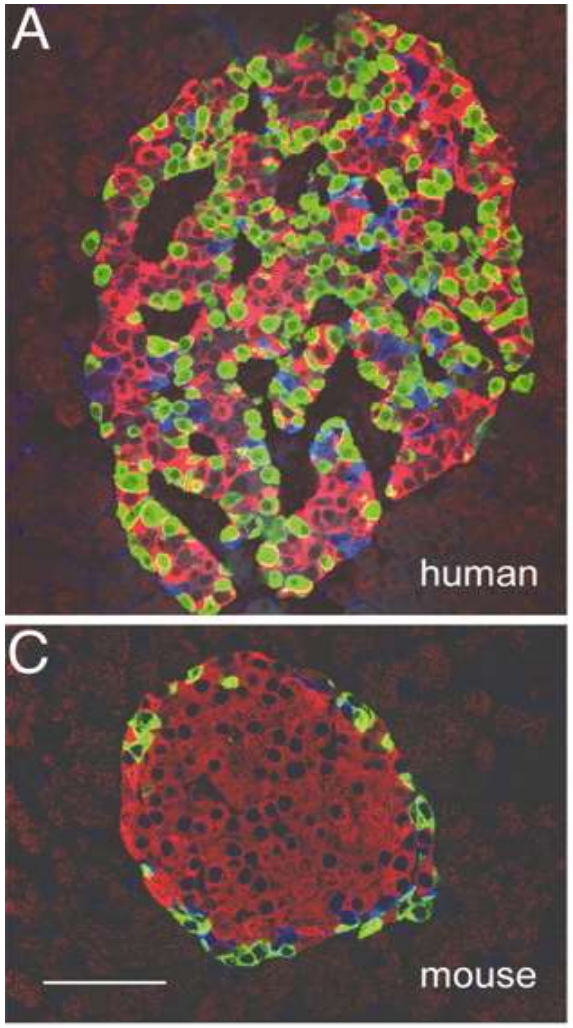
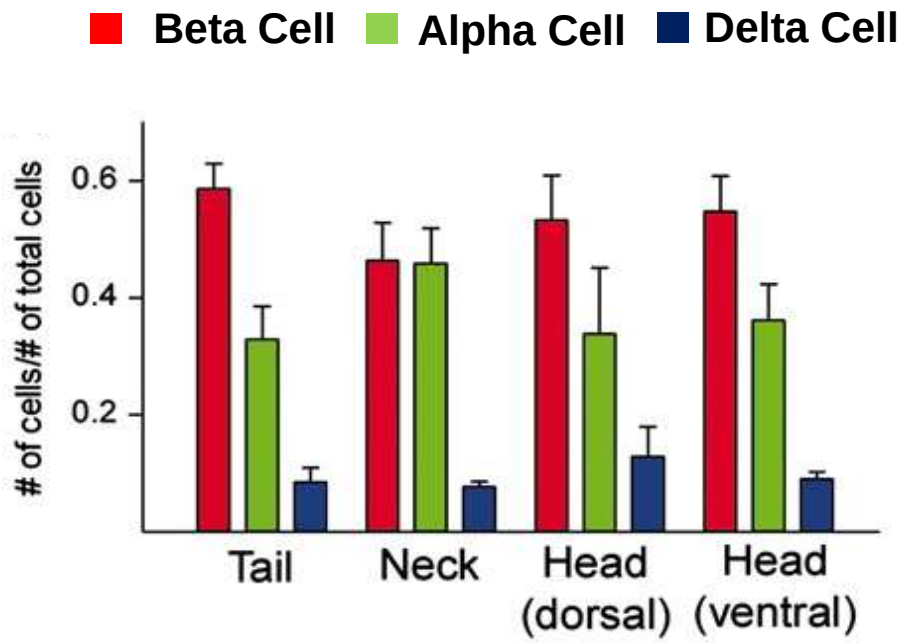
Organs-on-Chips

Microfluidic devices for culturing cells in perfused chambers to model physiological functions of tissues and organs

Islets of Langerhans - Interspecies Differences

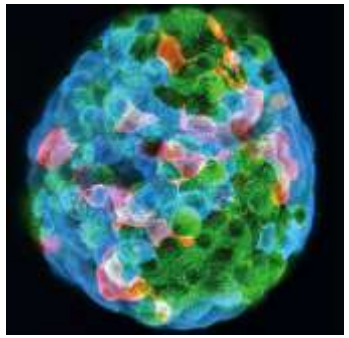




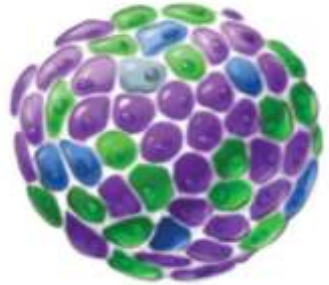
Human Islets

Cabrera et al., PNAS. 2006 Feb 14;103(7):2334-9

Cadaveric Islets



Stem Cell Islets

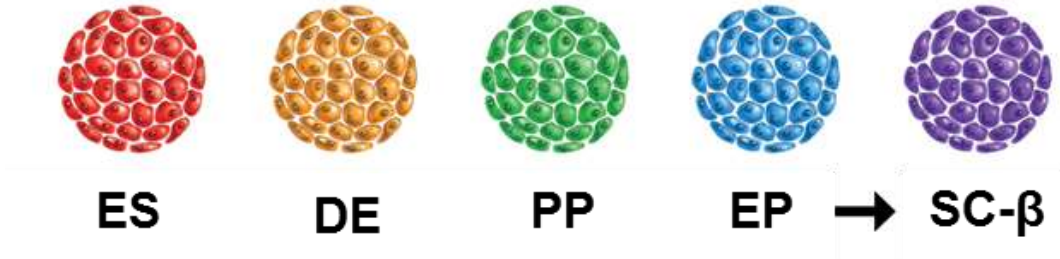


Cadaveric Islets	Stem Cell Islets
Diverse genetic background	Controlled genetic background
Low availability	Unlimited supply
Variable size	Controlled size
Variable composition	Controlled composition
Harsh isolation procedure	Grown in controlled environment

SC Beta Differentiation

SC-Beta Cells:

35 – 40 Day Differentiation Protocol



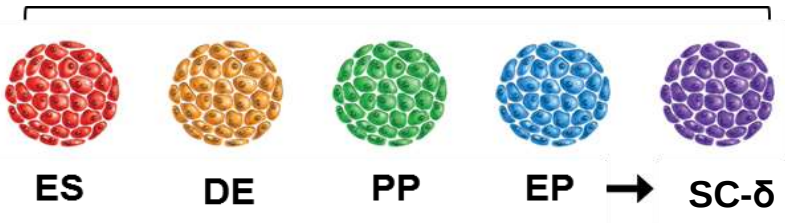
7 – 18 Days

S6 SC-β Cluster

SC-Alpha Cells:

SC-α Cluster

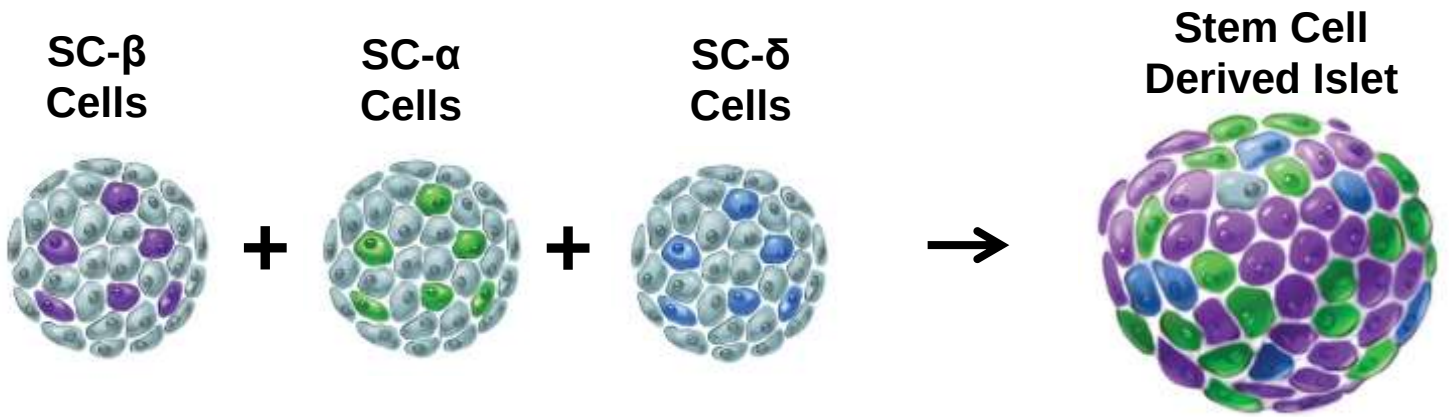
SC-Delta Cells:

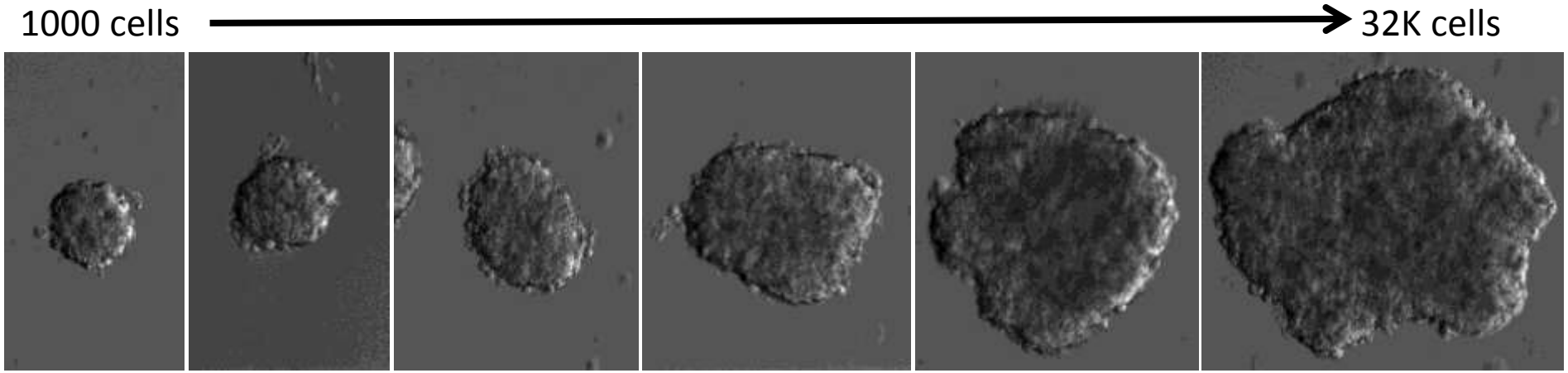


SC-δ Cluster

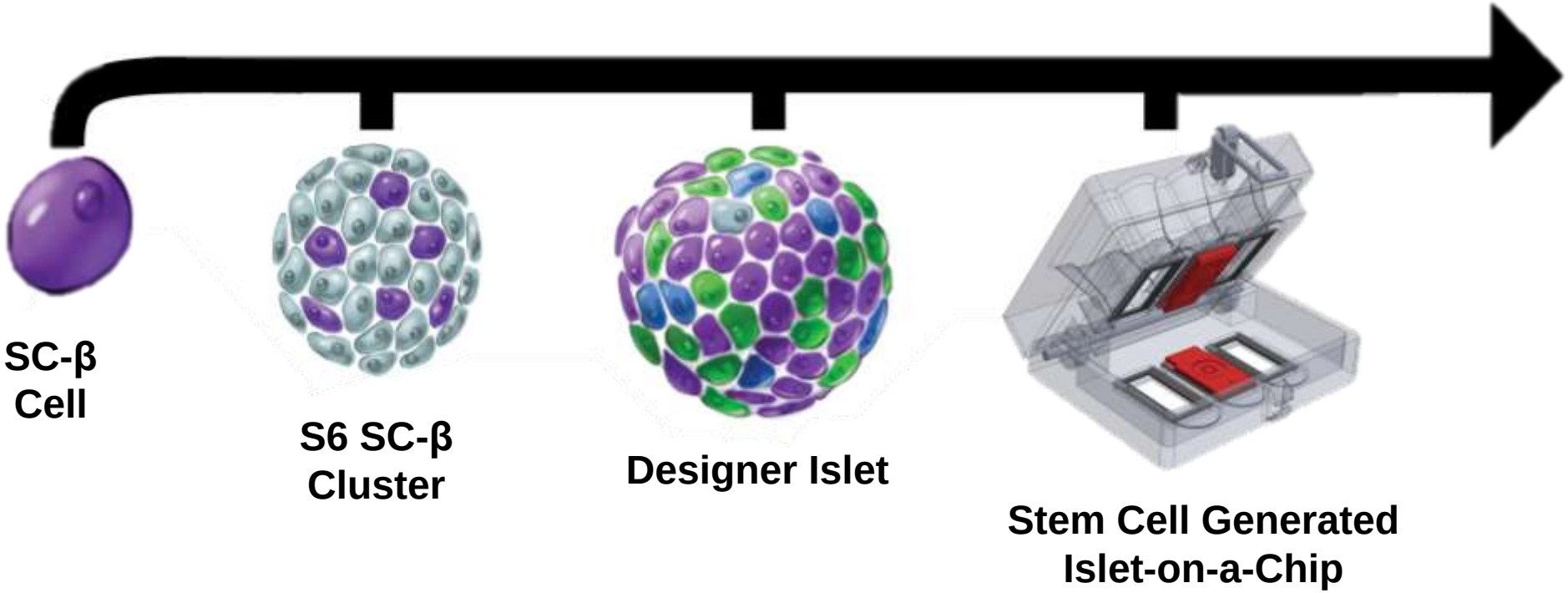
Differentiated and maintained in spinner flask culture

Engineering a Designer Islet

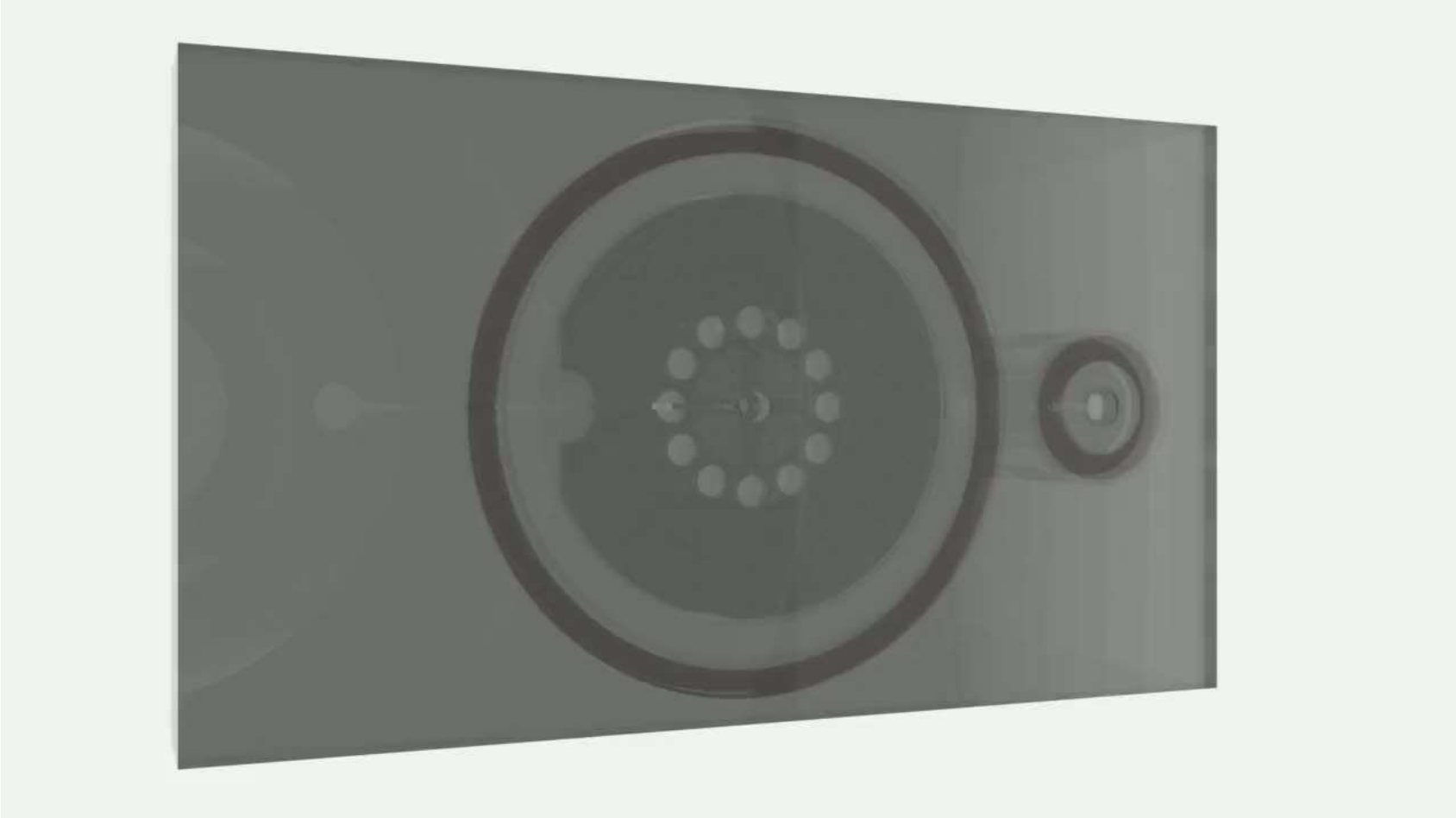




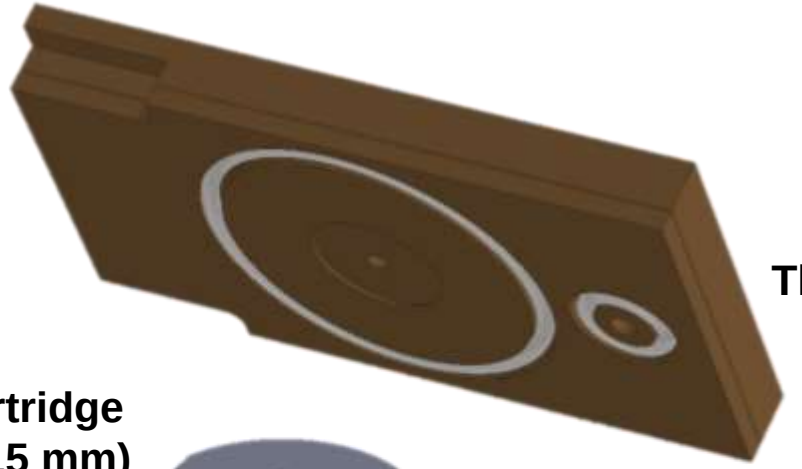
Poster: Quinn Peterson, Session I Wed. March 8


SC-β Cell
S6 SC-β Cluster
Designer Islet
Stem Cell Generated Islet-on-a-Chip

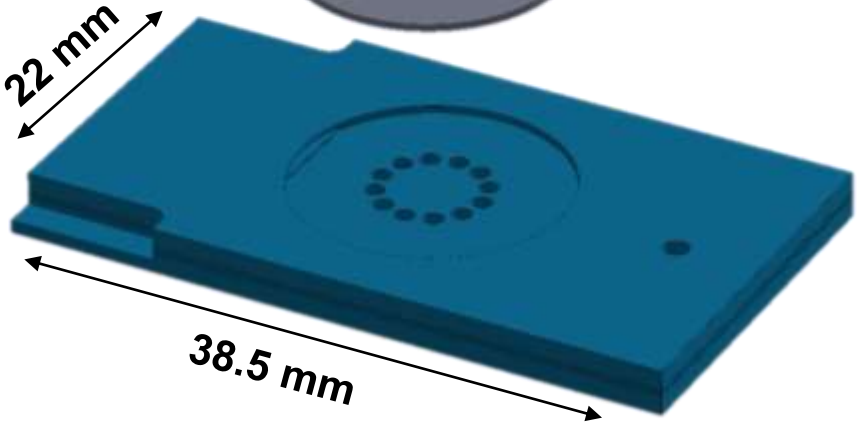
Pancreatic Islet Chip



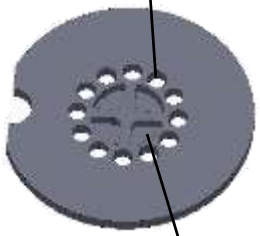
Pancreatic Islet Chip



Cartridge
(Ø15 mm)

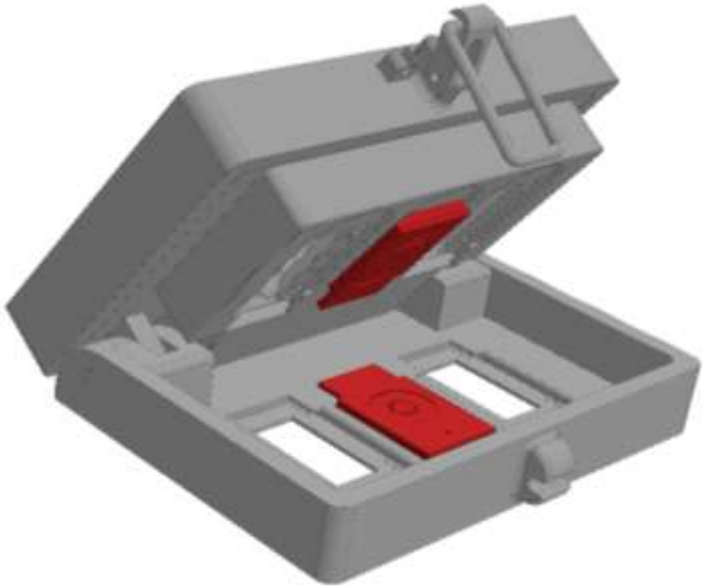


Through holes for
fluid flow



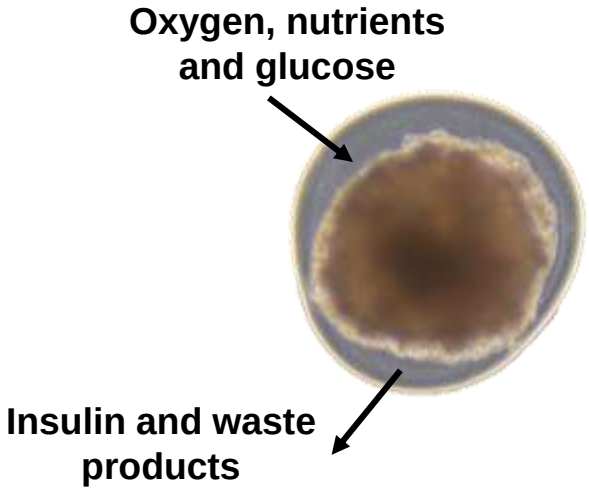
Quadrants
(house cell clusters)

Chip holder and clamping system

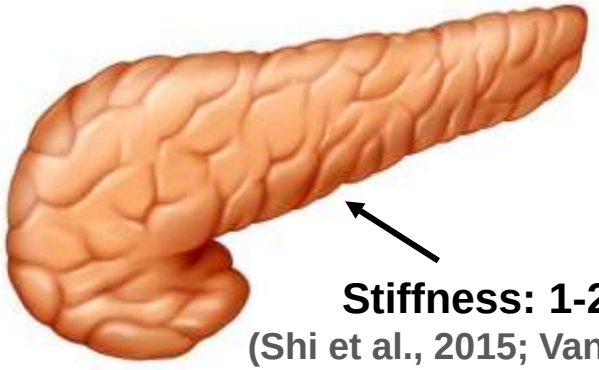


Chip Demo: Session I Wed. March 8

Housing Cells on Chip



Adapted from Tomei et al.,2015

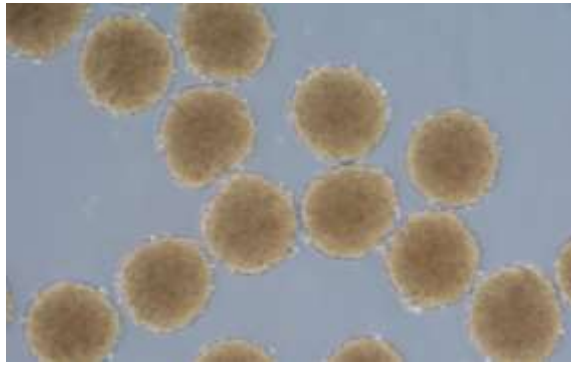


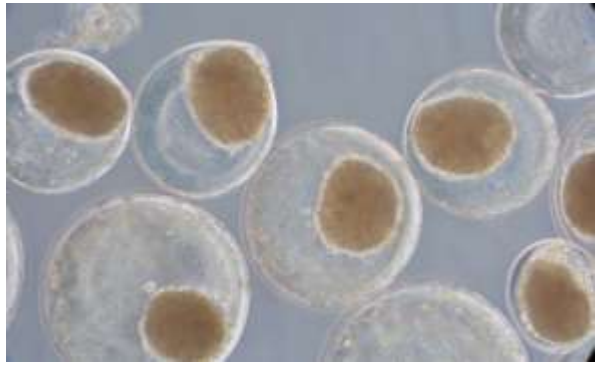
Stiffness: 1-2 kPa

(Shi et al., 2015; Vankatesh et al., 2015)

Factors to control cell housing:

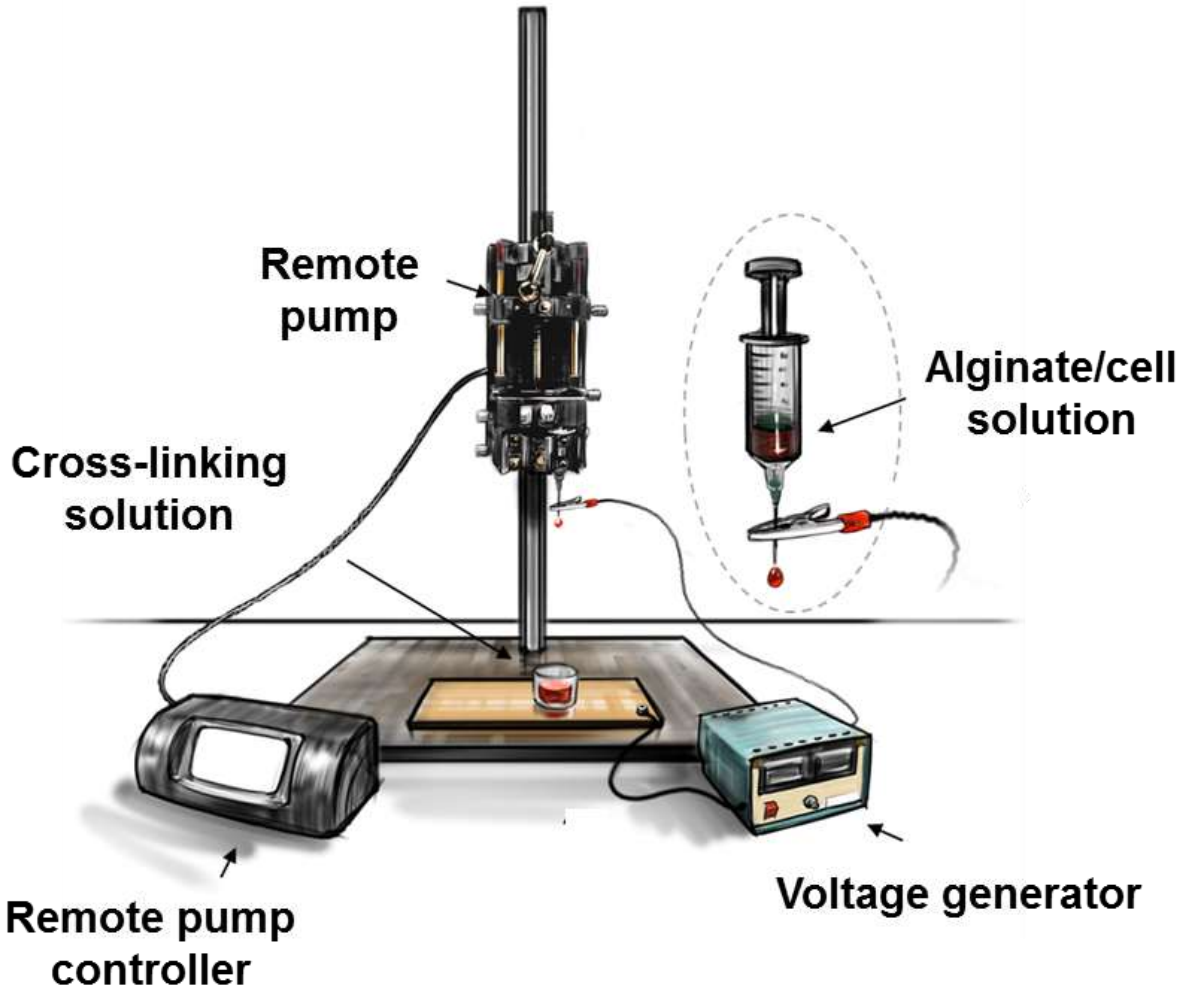
1. **Protection from hydrodynamic forces**
2. **Sufficient transport of oxygen, nutrients & secretory molecules**
3. **Enables incorporation of islet ECM proteins**
4. **Enables control of a defined micro-environment**
   - **Capsule diameter**
   - **Mechanical stability/stiffness**

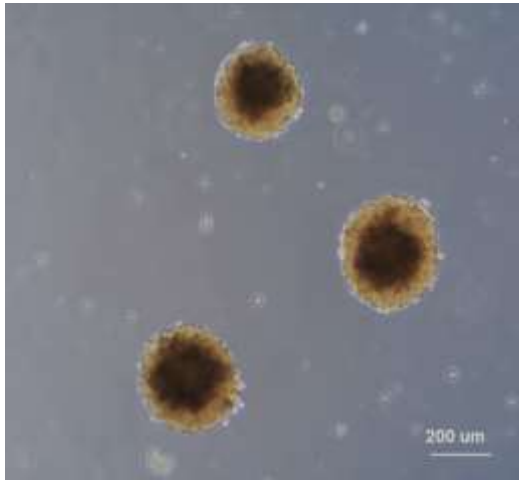




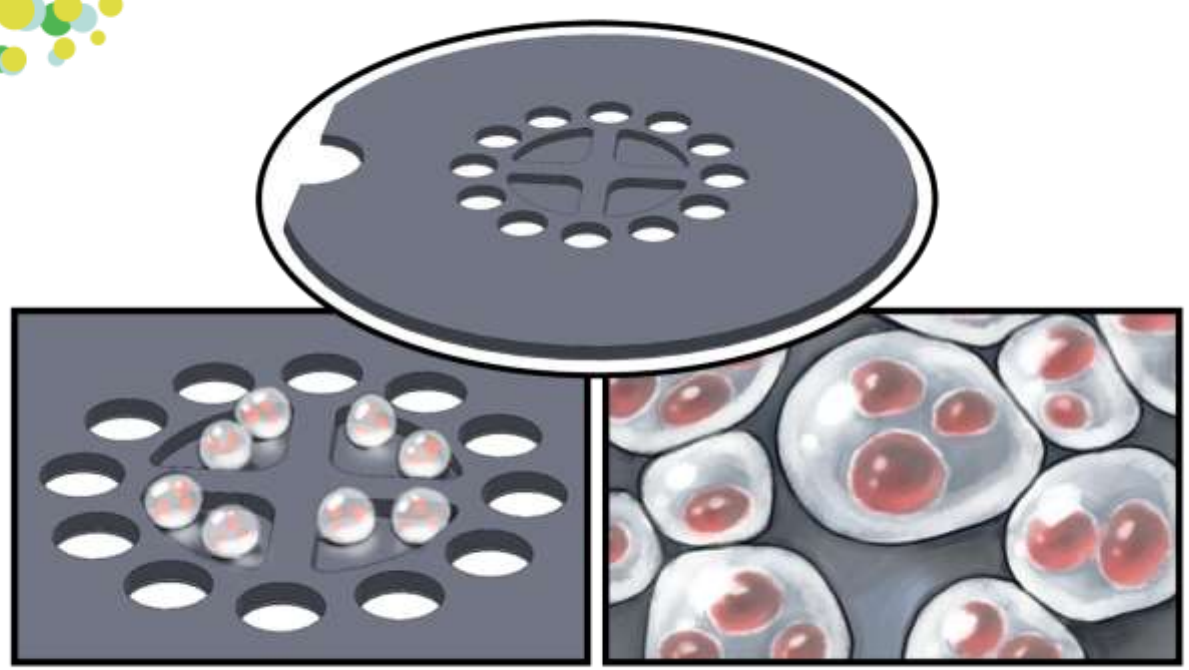
Housing Cells on Chip

Hydrogel Micro-encapsulation





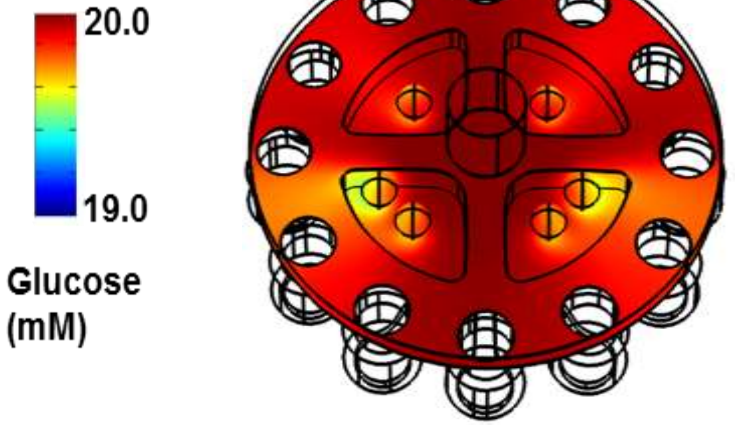
Mathematical Model



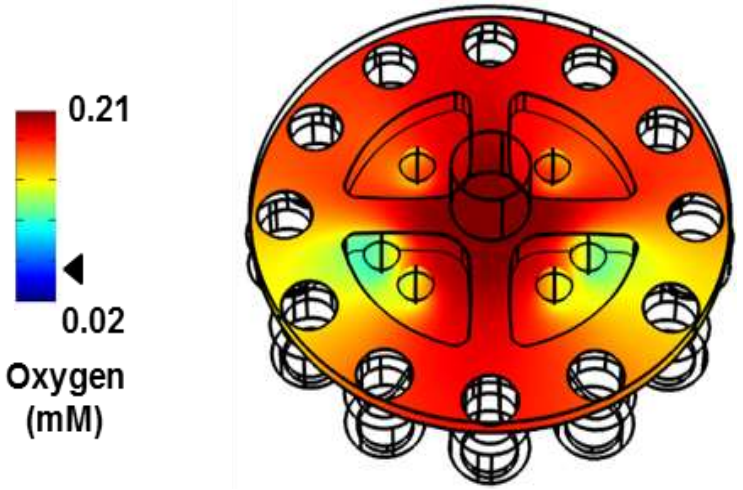
- Seeded with six 250 µm islets
- Micro-encapsulated in 125 µm layer
- Arrow (◀) represents lowest physiologically-relevant level (0.05 mM)*

*Dionne et al. (Diabetes) 1993;42(1):12-21

GLUCOSE CONCENTRATION PROFILE



OXYGEN CONCENTRATION PROFILE

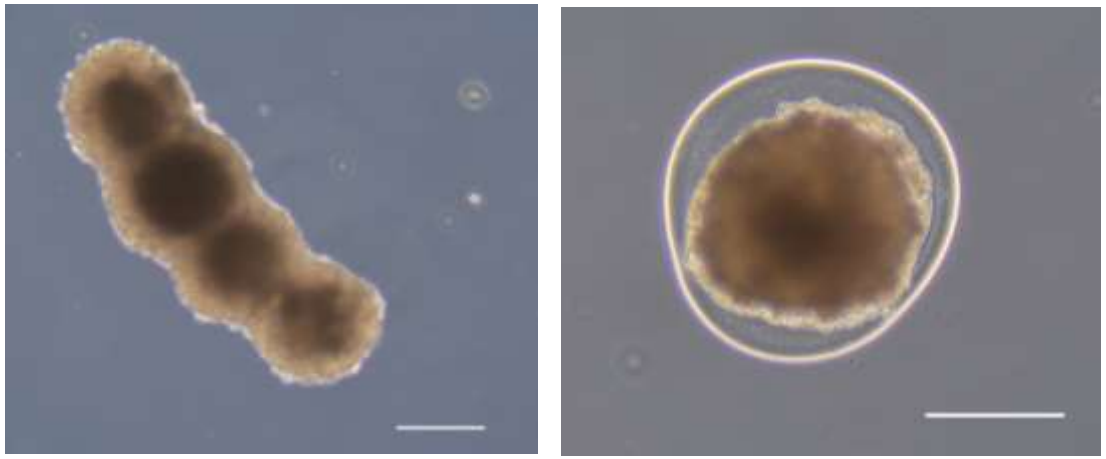


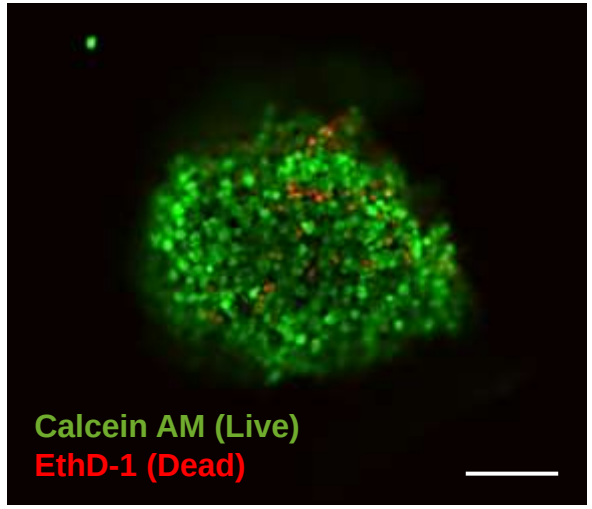
Structural Maintenance & Viability

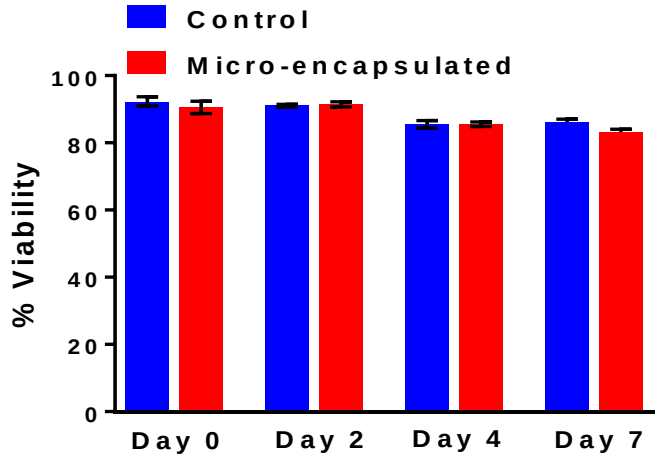
After 7 days in static culture:

Day 0

Day 7

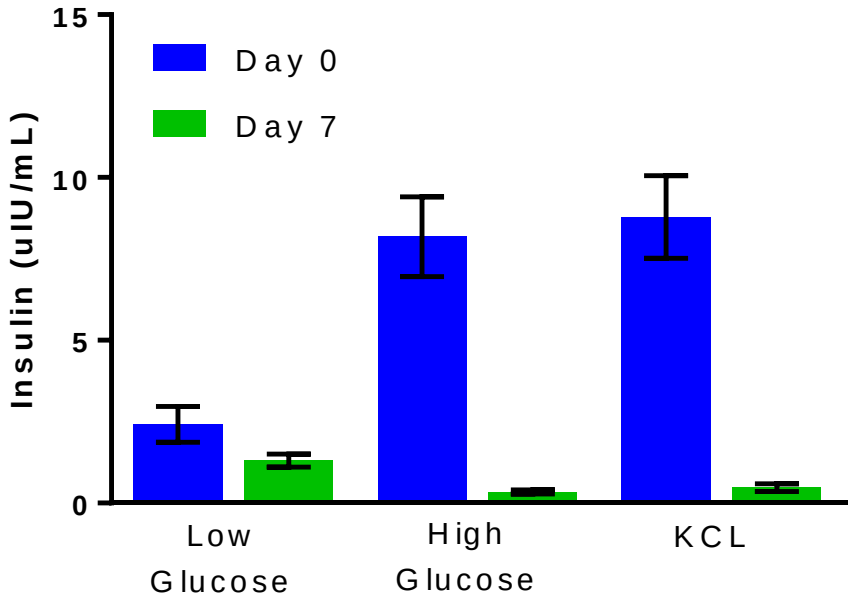






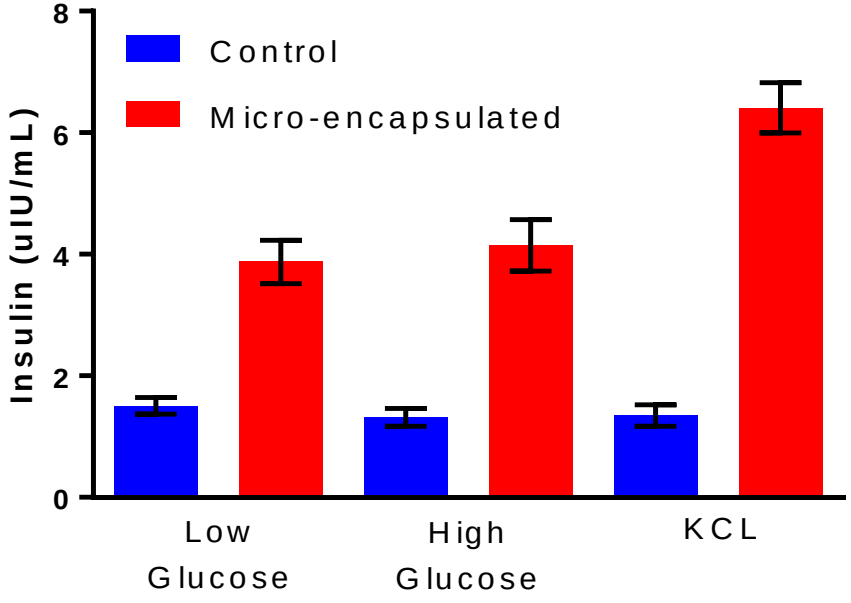
Cell Function

Human Islets

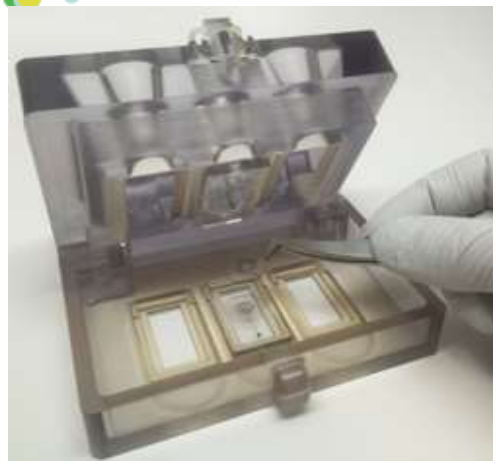


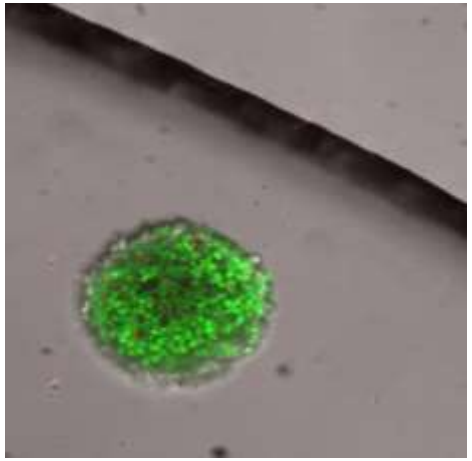
After 7 days in static culture:

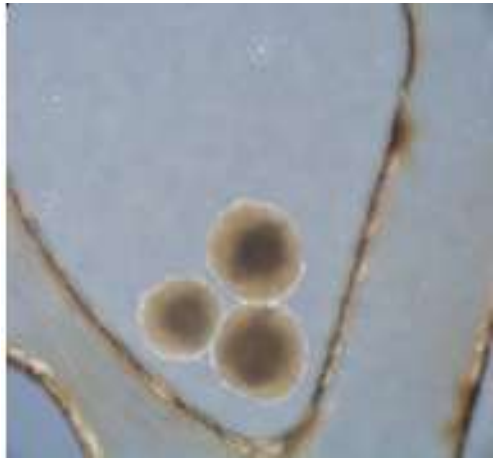
SC Beta Cells

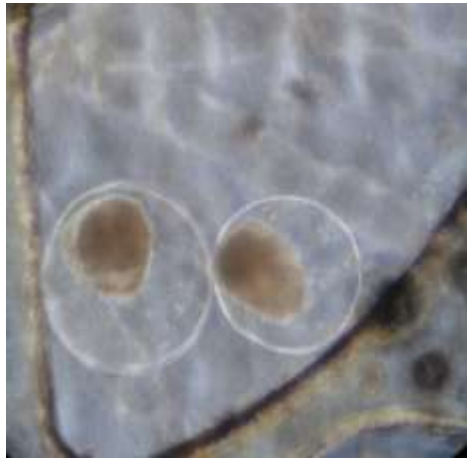


On Chip Functional Analysis





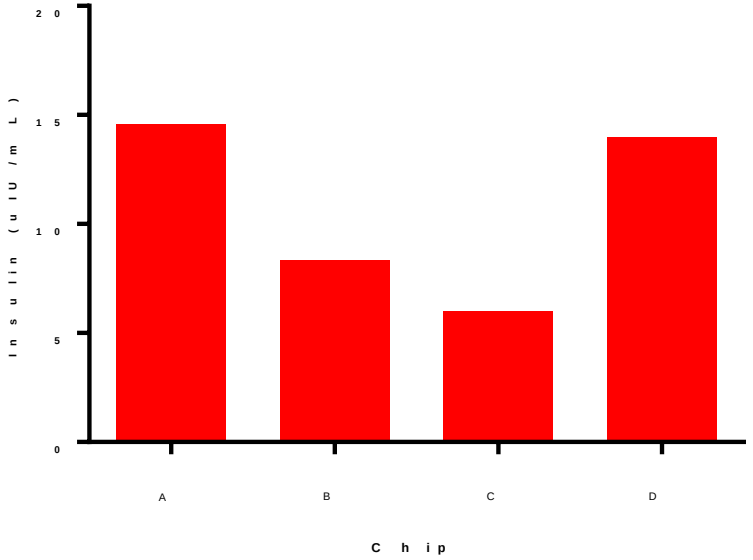




Control
Naked SC-β Clusters

Micro-encapsulated
SC-β Clusters

- **Maintain cells on chips for 7 days**
- **Perform on chip GSIS**
- **Continuously collect small volumes of supernatant**

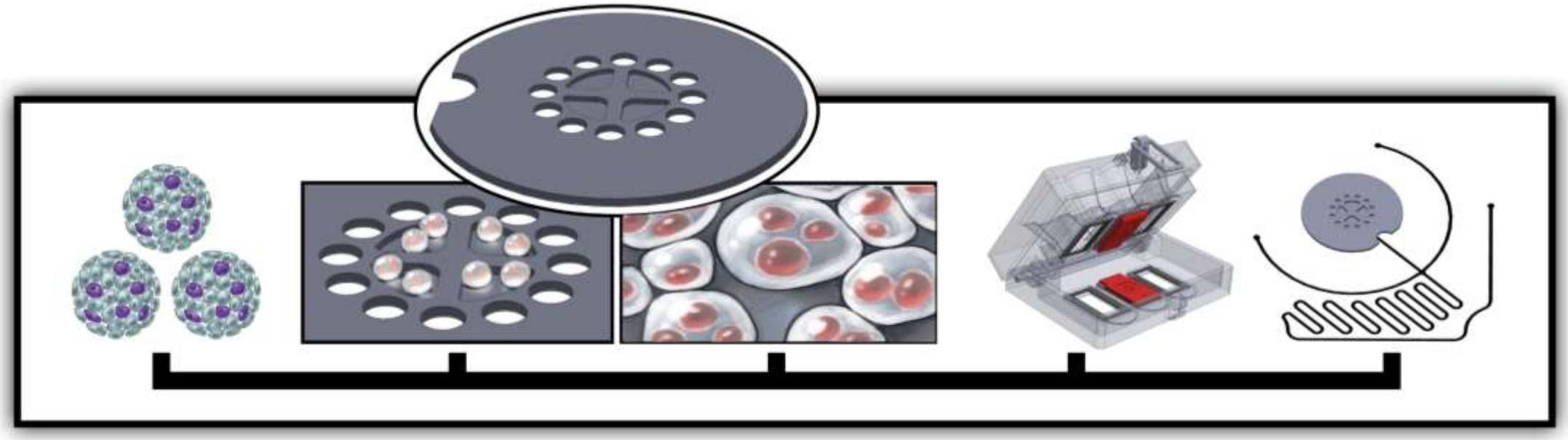


Moving Beyond ELISA For Insulin Measurement

Design Criteria	ELISA	Goal
On-Chip	NO	YES
Real-Time	NO	YES
Multi-Analyte	NO	YES
Low-Cost	NO	YES

Poster: Benjamin Pope, Session II Thurs. March 9

Looking Forward



Thank you

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Alex Cho

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Quinn Peterson, Ph.D.

Disease Biophysics Group