Shipping Human Islets

ICR WORKSHOP
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Rationale for Shipment Equipment

• There is a need for shipment of human islets from isolation centers to other facilities for research or clinical transplantation

• Containers currently used for islet shipment are inadequate as they may allow exposure of the islets to “deadly”:
  - temperature and pressure variations
  - Oxygen limitations
HUMAN ISLET SHIPPING

Important Parameters:

1. Temperature
2. Pressure
3. Oxygen

Data to support this?
Temperature Measurements During Shipping (March 2004)
Pressure Measurements During Shipping
(March 2004)
Effect of freezing temperature on viability

“Shipped” cells were exposed to temperatures below 0°C for more than 1 hr.
PO$_2$ = 130 mm Hg
Ambient PO$_2$ = 142 mm Hg
Medium Depth = 6 mm
Islet Diameter, D = 200 $\mu$m

Islets in Culture

Single Islet

Multiple Islets

d = 400 $\mu$m

(Avgoustiniatos E.S., MIT, Ph.D. Thesis, 2001)
Islets shipped pelletized in the bottom of centrifuge tubes are severely damaged.

**Petri dish**
- Air: 37°C
- Petri dish: Air: 37°C

**Pellet**
- Air: 24°C
- Pellet: Air: 24°C

**Porcine**
- n=4

**Rat**
- n=4
New Equipment for Islet Shipment
Hypothesis

Improving oxygenation by culturing islets on top of silicone rubber membranes will enable high-density culture (and shipment) without loss of viability
Hypothesis

Improving oxygenation by culturing islets on top of silicone rubber will enable high-density culture without loss of viability.
Culture Devices Based on Silicone Rubber

10 cm² GP Device

100 cm² GP Device

GP Silicone Rubber Membrane
Gas Permeable Bags

Gas permeable membranes differ.....
Avgoustiniatos et al., Xenotransplantation 14:420, 2007

- 97-137 times higher at 22 °C
- 66-84 times higher at 37 °C
Avgoustiniatos et al., Xenotransplantation 14:420, 2007

Oxygen Transmission Rate (cc/100 in²·day)

- Am. Fluoroseal VueLife 2PF-0290 (FEP)
- Baxter Lifecell (Polyolefin Blend)
- OriGen Permalife Series (FEP)
- Wilson-Wolf PR-5-0003-2 (Silicone Rubber)

Temperature:
- 22 °C
- 37 °C
Does it matter?
Anoxic Anoxic Anoxic Anoxic

147 mm Hg (Air)

Permalife Bag (127 μm = 0.005” Thick)

3 mm Hg

T = 22°C
3000 IE/cm²
T = 22°C, 3000 IE/cm²

Avgoustiniatos et al., Xenotransplantation 14:420, 2007
Pressure Regulated Gyroscopic Shipping Container for Silicone Rubber Vessels

* Gyroscope can minimize chances of islet accumulation/aggregation
Pressure Regulated Gyroscopic Shipping Container
Inside Styrofoam Box with Phase Change Material (PCM)*

*For Temperature Regulation
Results with PCM Loaded Box

Temperature (°C) vs. Elapsed Time (Hours)

A

-20°C

B

40°C

- Experimental Container 1 w/ 21 PCM Units
- External Temperature
- Experimental Container 2 w/ 2 TS Units
Results with Pressure regulated Shipping container
Combination of Approaches: Silicone Rubber with Enhanced Ambient pO₂

In collaboration with Giner Inc., NIH SBIR Phase II Project, and WW
Giner Portable Islet Culture System with temperature control using a modified thermoelectric chest (Vector 210®)
Test Shipment GINER-UMN
No Islets
Conclusions

• Successful implementation of simple cost-effective approaches can lead to substantial improvements in islet quality for research and clinical transplantation post-shipment

• More sophisticated approaches (Giner EOG) can provide finer level of control as needed
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