Clonetics™ Cells in Pancreatic Cancer Research

1 April 2014 / Speaker: Andrew Winner
2 April 2014 / Speaker: Dr. Nazim El-Andaloussi
Outline

- Introduction to Pancreatic Cancer
- Differences Between Primary Cells and Cell Lines
- Research Breakthroughs and Challenges
- Benefits of Clonetics™ Pancreatic Islets
- Custom Products for Pancreatic Research
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Pancreatic Cancer Research Market

- Fourth leading cause of cancer deaths\(^1\)
- Median survival time < 6 months\(^1\)
- Challenging early stage detection
- NCI supports development of new treatments\(^2\)

1. Howard, 1966; Parker, 1996; Greenlee et al., 2000
2. Elekta
Pancreatic Cancer Types

- Neuroendocrine tumors (NET)
  - Endocrine cancer – Tumorous islets

- Ductal adenocarcinoma
  - Exocrine Cancer

- Acinar cell carcinoma
  - Rare malignant tumor; poor prognosis
Primary Cell Types

Endocrine Region

- Pancreatic islets – Alpha, beta cells, delta, PP, Epsilon
- 1 to 2% of pancreas

Exocrine Region

- Acinar, ductal, centroacinar, stem cells
- Acinar cells – 85% of pancreas
- Ductal cells – 10% of pancreas
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# [Normal] Primary Cells vs. Pancreatic Cell Lines

<table>
<thead>
<tr>
<th></th>
<th>Primary Cells</th>
<th>Cell Lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Islet Substitutions</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Mutation Rate</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Tissue Representation</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Characterization Need</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Costs – Sample Number</td>
<td>↓</td>
<td>↑</td>
</tr>
</tbody>
</table>
Concerns About Cell Lines

- NIH - authentication of cultured cell lines **critical** for grant\(^1\)
- Some journals mandate characterization before publication
- 18-36% cell lines misidentified or cross-contaminated\(^2\)
- “Discrepancies exist...for...phenotype and genotype of pancreatic cell lines to warrant careful scrutiny...and thorough application of appropriate controls...”\(^3\)

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1. Notice Number: NOT-OD-08-017 <grants.nih.gov/grants/guide/notice-files/NOT-OD-08-017.html>
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Recent Research Breakthroughs

- First Human Model of Cancer Progression – PSC’s from Pancreatic Cancer Cells

- Discovery of cancer stem cells in pancreatic tumors helps understand pancreatic cancer development

Current Research Challenges

- Inconsistent literature on characterization profile of pancreatic cell lines\textsuperscript{1} 
- Limited cell line options for human islets\textsuperscript{2} 
- Limited access to normal primary human islets for research use  
- Limited access to early-stage donor-cells\textsuperscript{3} 
- Isolation difficulties of primary cell types from pancreas\textsuperscript{4} 

\textsuperscript{1} Pancreas. 2010 May; 39(4): 425–435  
\textsuperscript{2} Gordon C. Weir. Clin Invest. 2011;121(9):3395–3397  
\textsuperscript{3} Sharon Reynolds. Stem Cells Reveal Secrets About Cancer.\url{http://www.livescience.com/42402-stem-cells-cancer-research-nigms.html}  
\textsuperscript{4} M.J Smelt et. al. Experimental Diabetes Research Volume 2008 (2008), Article ID 165360, 11 pages
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Why Use Clonetics™ Human Pancreatic Islets?

- Human islet center that manufactures for clinical transplantation
- Fresh and frozen – Non-tumorous islets + acinar tissue
- Identity, quantity, purity, & viability testing
- Easy acquisition & steady supply
Why Use Clonetics™ Human Pancreatic Islets?

- Special donor characteristics
- Wilson Wolf Flask
- Growth Media included
- Technical Support
## Clonetics™ High-Quality Islets Preparations

Table: Characteristics of islet preparations and outcome of dynamic insulin function assay

<table>
<thead>
<tr>
<th>Characteristics of Islet Preparations</th>
<th>NHP (n=2)</th>
<th>Human (n=3)</th>
<th>AP (n=3)</th>
<th>JP (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purity (% dithizone stain)</td>
<td>83 ± 11</td>
<td>85 ± 13</td>
<td>90 ± 00</td>
<td>63 ± 19</td>
</tr>
<tr>
<td>OCR/DNA (nmol/min.mg DNA)</td>
<td>221 ± 57(h)</td>
<td>121 ± 12(^{nhp,ap,jp})</td>
<td>265 ± 25(^{h,jp})</td>
<td>188 ± 3.2(^{a,h,ap})</td>
</tr>
<tr>
<td>Total insulin (pg/ng DNA)</td>
<td>5.9 ± 0.9(^{jp})</td>
<td>7.8 ± 3.9(^{jp})</td>
<td>9.2 ± 3.4(^{jp})</td>
<td>1.5 ± 0.8(^{nhp,h,ap})</td>
</tr>
<tr>
<td>Insulin Secretory Function (AUC, pg insulin/ng DNA)</td>
<td>Glucose 1(^{st}) + 2(^{nd}) phase (16.7 mM)</td>
<td>335 ± 7(^{ap,jp})</td>
<td>348 ± 85(^{ap,jp})</td>
<td>121 ± 78(^{nhp,h,jp})</td>
</tr>
</tbody>
</table>

\(a\) OCR/DNA data were available for 3 of 4 cases in the JP group.

Data are presented as arithmetic means values ± SD.

Statistical significance (P < 0.05): \(^{nhp}\) compared with NHP; \(^{h}\) compared with human; \(^{ap}\) compared with AP; \(^{jp}\) compared with JP.
Human and mouse islets transduced dsAAV2-eGFP virus
Transduced islets were able to reverse diabetes *In Vivo*
Rat and human islets were transduced with different recombinant adenoviruses and assessed using immunobLOTS.
## Clonetics™ Fresh Human Pancreatic Islets

- Special donor characteristics subject to donor availability; turnaround times may vary

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Description</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>00201981</td>
<td>Fresh Human Pancreatic Islets, 100K</td>
<td>&gt;=100,000 IEQ</td>
</tr>
<tr>
<td>00201983</td>
<td>Fresh Human Pancreatic Islets, 20K</td>
<td>&gt;=20,000 IEQ</td>
</tr>
<tr>
<td>00201984</td>
<td>Fresh Human Pancreatic Islets, 10K</td>
<td>&gt;=10,000 IEQ</td>
</tr>
<tr>
<td>00201985</td>
<td>Fresh Human Pancreatic Islets, 5K</td>
<td>&gt;=5,000 IEQ</td>
</tr>
<tr>
<td>00202998</td>
<td>Fresh Human Pancreatic Islets, 2K</td>
<td>&gt;=2,000 IEQ</td>
</tr>
</tbody>
</table>
Clonetics™ Fresh Human Pancreatic Islets – Standard QC Testing

<table>
<thead>
<tr>
<th>Part Number</th>
<th>Test</th>
<th>Minimum Specs Guarantee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included</td>
<td>Islet Quantity</td>
<td>(IEQ Count)</td>
</tr>
<tr>
<td>Included</td>
<td>Islet Sterility</td>
<td>Gram Negative Stain on Day 0</td>
</tr>
<tr>
<td>Included</td>
<td>Islet Viability</td>
<td>[FDA/PI] (%) &gt;= 70%</td>
</tr>
<tr>
<td>Included</td>
<td>Islet Purity</td>
<td>&gt;= 70% islet cells vs. other tissue (based on visual representation)</td>
</tr>
</tbody>
</table>

- COA also includes age, sex, race & BMI of the donor
- Islets test negative for Hepatitis B, Hepatitis C & HIV-1
### Clonetics™ Fresh Human Pancreatic Islets – Additional QC Testing

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Test</th>
<th>Typical Results (F.I.O.)</th>
<th>Estimated Testing Time (Results Post-Shipment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>00202551</td>
<td>DNA Quantitation</td>
<td>12.9 +/- 6.9 mg DNA</td>
<td>1 day</td>
</tr>
<tr>
<td>00202552</td>
<td>Glucose Stimulated Insulin Response</td>
<td>4.1 +/- 2.8 fold</td>
<td>4 days</td>
</tr>
<tr>
<td>00202553</td>
<td>Oxygen Consumption Rate</td>
<td>123.4 +/- 23.1 pmol/min/μg DNA</td>
<td>1 day</td>
</tr>
<tr>
<td>00202540</td>
<td>Beta-Cell Composition</td>
<td>48.4 +/- 9.4%</td>
<td>14 days</td>
</tr>
</tbody>
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Cells on Demand™

Human
- Fresh or Frozen Normal Acinar Tissue
- Frozen Normal Islets

Pig, Monkey
- Fresh or Frozen Normal Islets and Acinar Tissue

For additional requests not listed above, please contact our Cells on Demand Service

Inquiries: CellsonDemand@lonza.com
Lonza Cancer Product Portfolio

- Clonetics™ and Poietics™ Cells and Media tested and guaranteed to perform
  [www.lonza.com/primary](http://www.lonza.com/primary)
  - Primary cells from pancreatic, bone, blood, lymph, lung, mammary and other tissue types
- Nucleofector™ Technology for transfection of primary cells and cancer cell lines
- Clonetics™ Conditionally Immortalized Cell Lines (CCICs)
- Biowhittaker™ Liquid and Powder Media for cancer research and therapeutic applications
- Nucleic Acid and Protein Electrophoresis Products
Summary

- Restricted access to normal primary human islets and limited cell line options for research use

- Lonza’s Clonetics™ Human Pancreatic Islets
  - Fresh or frozen
  - Steady supply
  - Guaranteed quality
  - Flexibility

- Lonza’s Cells on Demand™ Service
  - Acinar tissue
  - Pancreatic cells from animal species
How to Order or Pose Questions

Order queries:
- U.S: 800 638 8174 (toll free) or order.us@lonza.com
- Europe: +32 87 321 611 or order.europe@lonza.com

Scientific support:
- U.S: +1 800 521 0390 or scientific.support@lonza.com
- Europe: +32 87 321 611 or scientific.support.eu@lonza.com

Web address: www.lonza.com/islets for more information
Interested to Learn More?

- Join our upcoming webinar:

  - Efficient Transfection of Biologically Relevant Cells in Immunology Research
    
    Slot 1: Tuesday, 13 May 2014
    2 PM EDT (New York) / 11 AM PDT (Los Angeles)

    Slot 2: Wednesday, 14 May 2014
    10 AM CEST (Berlin) / 9 AM BST (London) / 5 PM JST (Tokyo)

- Register at: www.lonza.com/webinar16
Thank You for Your Kind Attention