Blastocyst complementation generates exogenic pancreas in vivo in apancreatic cloned pigs

Hitomi Matsunari\textsuperscript{a,b,c,1}, Hiroshi Nagashima\textsuperscript{a,b,c,1}, Masahito Watanabe\textsuperscript{b,c}, Kazuhiro Umeyama\textsuperscript{b,c}, Kazuaki Nakano\textsuperscript{c}, Masaki Nagaya\textsuperscript{b,c}, Toshihiro Kobayashi\textsuperscript{a}, Tomoyuki Yamaguchi\textsuperscript{a}, Ryo Sumazaki\textsuperscript{d}, Leonard A. Herzenberg\textsuperscript{e,2}, and Hiromitsu Nakauchi\textsuperscript{a,f,2}

\textsuperscript{a}Japan Science and Technology Agency, Exploratory Research for Advanced Technology, Nakauchi Stem Cell and Organ Regeneration Project, Chiyoda-ku 102-0075, Japan; \textsuperscript{b}Meiji University International Institute for Bio-Resource Research, Kawasaki 214-8571, Japan; \textsuperscript{c}Laboratory of Developmental Engineering, Department of Life Sciences, School of Agriculture, Meiji University, Kawasaki 214-8571, Japan; \textsuperscript{d}Department of Gene Therapy, National Institute of Health, Tsukuba 305-8575, Japan; \textsuperscript{e}Department of Gene Therapy, Center for Stem Cell Biology and Medicine, Institute of Biomaterials and Bioengineering, University College London, London W1N 8AA, United Kingdom; \textsuperscript{f}Department of Developmental Biology, University of Tokyo, Tokyo 113-8656, Japan.
What was the main objective of this paper?

Determine if transplant of pancreatic competent pluripotent stem cells into apancreatic embryos would give rise to animals that have pancreases derived wholly from transplanted cells in pigs.

Why in the world would you want to do this?
To create a ready supply of organs for recipients
Need for Organs for Transplant

Every day an average of 79 people receive organ transplants.

Every day an average of 18 people die while waiting for transplants that don't happen because of a shortage of donated organs.
Need for Organs for Transplant

THE WIDENING GAP

http://healthresearchfunding.org
How Long is the Wait

MEDIAN NATIONAL WAITING TIME

- Hearts: 113 days
- Lungs: 141 days
- Livers: 361 days
- Kidneys: 1,219 days
- Pancreata: 260 days
- Intestine: 159 days

PERCENTAGE OF RECIPIENTS WHO WERE LIVING 5 YEARS AFTER THEIR TRANSPLANT (2009):

- Lung: 54.4%
- Heart: 74.9%
- Kidney: 69.3% 73.8%
Organ Transplants Save Lives

1 donor can save up to 8 lives

HOW LONG CAN ORGANS SURVIVE?
Matching organs must be done quickly -- not only for the health of the recipient, but some organs must be transplanted in a matter of hours.

- Heart: 4-6 hours
- Lungs: 4-8 hours
- Kidneys: 36-48 hours
- Livers: 12-15 hours

http://healthresearchfunding.org
What Can Be Donated

DECEASED DONORS

ORGANS
- Heart
- Intestines
- Kidneys
- Pancreas
- Liver
- Lungs

TISSUES
- Veins
- Heart Valves
- Cartilage
- Tendons & Ligaments
- Corneas
- Middle Ear
- Skin
- Bone

LIVING DONORS

ORGANS
- Kidney
- Liver
- Pancreas
- Lung
- Intestine

TISSUES
- Eye
- Skin

STEM CELLS
- Marrow
- Peripheral Blood Stem Cells
- Cord Blood Stem Cells
- Blood & Platelets

http://healthresearchfunding.org
Problems of Organ Transplant
# Problems of Organ Transplant

## Table 2: Estimated U.S. Average 2014 Billed Charges per Transplant

<table>
<thead>
<tr>
<th>Transplant Type</th>
<th>30 Days Pre-Transplant</th>
<th>Procurement</th>
<th>Hospital Transplant Admission</th>
<th>Physician During Transplant</th>
<th>180 Days Post-Transplant Discharge</th>
<th>Op Immuno-Suppressants and Other Rx</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single-Organ/Tissue</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow - Allogeneic</td>
<td>$57,600</td>
<td>$55,700</td>
<td>$479,600</td>
<td>$23,400</td>
<td>$290,300</td>
<td>$24,000</td>
<td>$930,600</td>
</tr>
<tr>
<td>Bone Marrow - Autologous</td>
<td>$56,300</td>
<td>$10,700</td>
<td>$212,300</td>
<td>$10,800</td>
<td>$81,800</td>
<td>$6,100</td>
<td>$378,000</td>
</tr>
<tr>
<td>Cornea</td>
<td>0</td>
<td>0</td>
<td>20,000</td>
<td>8,600</td>
<td>0</td>
<td>0</td>
<td>28,600</td>
</tr>
<tr>
<td>Heart</td>
<td>$50,800</td>
<td>$97,200</td>
<td>$771,500</td>
<td>$88,600</td>
<td>$198,400</td>
<td>$35,600</td>
<td>$1,242,200</td>
</tr>
<tr>
<td>Intestine</td>
<td>$78,900</td>
<td>$92,100</td>
<td>$552,900</td>
<td>$112,400</td>
<td>$272,700</td>
<td>$38,200</td>
<td>$1,547,200</td>
</tr>
<tr>
<td>Kidney</td>
<td>$23,200</td>
<td>$44,400</td>
<td>$119,800</td>
<td>$20,500</td>
<td>$66,800</td>
<td>$19,800</td>
<td>$334,300</td>
</tr>
<tr>
<td>Liver</td>
<td>$37,300</td>
<td>$95,000</td>
<td>$399,100</td>
<td>$53,100</td>
<td>$128,900</td>
<td>$25,700</td>
<td>$739,100</td>
</tr>
<tr>
<td>Lung - Single</td>
<td>$21,800</td>
<td>$90,200</td>
<td>$435,200</td>
<td>$44,600</td>
<td>$165,800</td>
<td>$27,400</td>
<td>$785,000</td>
</tr>
<tr>
<td>Lung - Double</td>
<td>$30,700</td>
<td>$129,700</td>
<td>$566,900</td>
<td>$59,100</td>
<td>$219,800</td>
<td>$31,500</td>
<td>$1,037,700</td>
</tr>
<tr>
<td>Pancreas</td>
<td>$12,100</td>
<td>$93,800</td>
<td>$104,300</td>
<td>$18,800</td>
<td>$67,700</td>
<td>$20,800</td>
<td>$317,500</td>
</tr>
<tr>
<td><strong>Multiple-Organ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart-Lung</td>
<td>$88,500</td>
<td>$168,700</td>
<td>$1,607,100</td>
<td>$108,700</td>
<td>$304,200</td>
<td>$36,400</td>
<td>$2,313,800</td>
</tr>
<tr>
<td>Intestine with Other Organs</td>
<td>$88,600</td>
<td>$236,400</td>
<td>$1,045,400</td>
<td>$132,800</td>
<td>$297,400</td>
<td>$44,100</td>
<td>$1,844,700</td>
</tr>
<tr>
<td>Kidney-Heart</td>
<td>$76,100</td>
<td>$136,000</td>
<td>$1,162,100</td>
<td>$132,500</td>
<td>$296,500</td>
<td>$37,100</td>
<td>$1,840,300</td>
</tr>
<tr>
<td>Kidney-Pancreas</td>
<td>$35,000</td>
<td>$123,300</td>
<td>$227,000</td>
<td>$35,200</td>
<td>$114,700</td>
<td>$22,500</td>
<td>$558,600</td>
</tr>
<tr>
<td>Liver-Kidney</td>
<td>$60,800</td>
<td>$161,500</td>
<td>$644,500</td>
<td>$86,700</td>
<td>$210,300</td>
<td>$26,500</td>
<td>$1,190,300</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-Organ</td>
<td>$76,700</td>
<td>$177,600</td>
<td>$926,100</td>
<td>$116,500</td>
<td>$288,600</td>
<td>$35,300</td>
<td>$1,620,800</td>
</tr>
</tbody>
</table>

[http://www.transplantliving.org](http://www.transplantliving.org)
Problems of Organ Transplant

Immune Rejection

Get Lost.
Problems of Organ Transplant

Immunosuppressive Drugs
Challenges in Attempting to Grow Organs Outside of the Body
Challenges in Attempting to Grow Organs Outside of the Body

Vascularization of Organ

Nervous System in Organs
Organ Transplants in Pets

• The only type of organ transplant available right now for pets is a kidney transplant

• Dogs are more likely to reject a donor kidney unless it comes from a related dog

• For cats, there is no need for the donor and recipient to be related as long as blood cross matches
Organ Transplants in Cats

The three options for finding a donor cat are:

1. If you have another cat in your household who is young and healthy

2. Finding a donor cat at a shelter (and then adopting that cat after the transplant)

3. Contacting a research vendor to order a cat who was bred for the purpose of being a donor
What was the main objective of this paper?

Determine if transplant of pancreatic competent pluripotent stem cells into apancreatic embryos would give rise to animals that have pancreases derived wholly from transplanted cells in pigs.

Why in the world would you want to do this?
How Can This Potentially Work For Humans?
Our Friend the Pancreas

The pancreas /ˈpæŋkriəs/ is a glandular organ in the digestive system and endocrine system of vertebrates. In humans, it is located in the abdominal cavity behind the stomach. It is an endocrine gland producing several important hormones, including insulin, glucagon, somatostatin, and pancreatic polypeptide which circulate in the blood. The pancreas is also a digestive organ, secreting pancreatic juice containing digestive enzymes that assist digestion and absorption of nutrients in the small intestine. These enzymes help to further break down the carbohydrates, proteins, and lipids in the chyme.
Figure 1

2 out of 5

acinar
Figure 2
Figure 3
Figure 4
What was the main conclusion of this paper?

They were capable of transplanting pancreatic competent pluripotent stem cells into apancreatic embryos that gave rise to animals with functional pancreases derived from transplanted cells in pigs.
Is There a Problem Transplanting Human Cells Into Pigs to Generate Chimeras?