Tissue Engineering

Part 1: Engineering Tissue Replacements

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The Need for Tissue Replacements

<table>
<thead>
<tr>
<th>Organ</th>
<th>Procedures/Yr (MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>4.75</td>
</tr>
<tr>
<td>Bone</td>
<td>1.34</td>
</tr>
<tr>
<td>Cartilage</td>
<td>1.15</td>
</tr>
<tr>
<td>Blood vessel</td>
<td>1.36</td>
</tr>
<tr>
<td>Tendon/Ligament</td>
<td>0.123</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.738</td>
</tr>
</tbody>
</table>

Langer & Vacanti, Science, 1993
Tissues Across Length Scales
Why a Bioengineered Tissue?

If one can improve upon:

• a device
• a drug
• a minimally-manipulated cell
• surgical reconstruction
• a transplant (unos.org)

• **Engineered tissues = biomaterials + cells**
  – Biomaterials that recruit cells (acellular)
  – Biomaterials that house cells (hybrid)
  – Biomaterial-free structures
    (hybrid w/ cell-derived ECM)

Vacanti, 1997 [image]
Small Intestine Submucosa (Acellular)

www.student.lore7o.org
Badylak and coworkers
Skin (Hybrid)

Engineered Skin | Human Skin

Organogenesis, Inc.
Bladder (Hybrid)

Tengion; Atala A et al; Lancet 2006: 367 124-6
Blood Vessel
(Biomaterial-free)

www.cytograft.com; L’Heureux, FASEB J, 1998
Blood Vessel
Designing bioengineered tissues I: Pick a function

<table>
<thead>
<tr>
<th>Organ</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Barrier</td>
</tr>
<tr>
<td>Kidney</td>
<td>Secretory</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Insulin production</td>
</tr>
<tr>
<td>Cartilage</td>
<td>Space filling</td>
</tr>
<tr>
<td>Bladder</td>
<td>Compliance</td>
</tr>
</tbody>
</table>
II: Pick ingredients & fabrication method

- **Raw Ingredients:**
  - Cells
    - Somatic (auto-, allo-, xeno-)
    - Stem cells
  - Biomaterials
  - Nutrients

- **Fabrication:**
  - Assembly
  - Bioprocessing
  - Preservation
Culturing Primary Cells

- Adult
- Embryo
- Egg

1. Dissection
2. Enzymatic digestion
3. Finely chopped
4. Further dissection
5. Primary cell culture
6. Explant culture
7. Organ culture
Hayflick Limit

Hayflick, 1965
Pluripotent Stem Cells

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Matching Degradation with Synthesis

Yannas & coworkers, PNAS, 1989; J&J and Cook Biotech
Synthetic Scaffolds

- PLGA, PCL
- PEG
- ePTFE
- Glycans
- Titanium
Natural Scaffolds

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Hierarchical Organization
Cellular Microenvironment

- Microenvironment Stimuli:
  - Soluble Factors
  - Cell-Cell Interactions
  - Cell-ECM Interactions
  - Physical Forces / Cell Shape

- Cell Fate:
  - Proliferation
  - Differentiation
  - Apoptosis
  - Migration

- Cell Function:
  - Biosynthesis / Metabolism
3D Tissue Environments

R. Sah: J Orthop Research, 2002
3-D Fabrication & Assembly
Bioreactor

Science.nasa.gov; Gottwald & coworkers
Cryopreservation

- Seeding of External Ice
- Slow Cooling
- Rapid Cooling

-1 to -4°C
<-10°C

Fowler & Toner, PNAS 2005
Conclusions

- Engineered tissue replacements combine cells & biomaterials to replace a subset of tissue functions
- Cells are derived from somatic cells or stem cells
- Biomaterials are natural or synthetic
- Tissue structure is hierarchical and therefore engineered tissue architecture must control microscale environment to control cell function
- Convergence of cell biology, medicine, and engineering is advancing the field