Stem Cells: Introduction and Prospects in Medicine

Bioscience in the 21st Century

Ware, 2011
Overview

• Setting the stage for a discussion about tissue engineering:
  
  Historical perspective
  
  Prospects in cell-based therapies (regenerative medicine - replacement of damaged or diseased cells and tissues with new cells and tissues) and drug screening

• Stem Cell Basics:
  
  What are stem cells?
  
  Where do stem cells come from?
  
  Types of stem cells:
    embryonic stem cells
    adult-derived stem cells
    induced pluripotent stem cells (iPSCs)

• Adult Stem Cell Advances in the News!
• Stem Cell Research Challenges
• Summary
Historical Perspective and Prospects for Regenerative Medicine
Historical Perspectives

• Major changes in cell-based therapies due to advances in stem cell technologies

• Some stem cell therapies in existence for over 50 years. First successful bone marrow transplant done in 1956 on leukemia patient. Bone marrow contains adult-derived hematopoietic stem cells (able to regenerate tissues similar to the specialized tissues in which they are found).

• Embryonic stem cells, adult stem cells, and induced pluripotent stem cells are believed to have great potential for regenerative medicine.
Development of induced pluripotent stem cells (iPSCs)

**2007 Nobel Prize in Medicine**

Mario R. Capecchi, Martin J. Evans and Oliver Smithies for their discoveries of the principles for introducing specific gene modifications in mice by the use of embryonic stem cells.

I. What are stem cells?
**Basic Characteristics of Stem Cells**

How do cells remain self-renewing and unspecialized?

1. **Self renew or**
2. **Differentiate** into a specialized cell type

**STEM CELL**

**What are the SIGNALS ???
Hormones
Growth factors
Small proteins**

**Stem cells properties:**
1. Capable of dividing and renewing for long periods
2. Are unspecialized.
3. Give rise to specialized cells.

Adapted from *Stem Cells and Cloning* by Kelly A. Hogan; http://stemcells.nih.gov/info/basics/basics2.asp
What distinguishes cell types from one another?
Protein Profiles Differ in Different Cell Types

**Figure from Stem Cells and Cloning by K.A. Hogan**

<table>
<thead>
<tr>
<th>Genes for...</th>
<th>Muscle cells</th>
<th>Pancreas cells</th>
<th>Blood cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolysis enzymes</td>
<td>On</td>
<td>On</td>
<td>On</td>
</tr>
<tr>
<td>Muscle contraction proteins</td>
<td>On</td>
<td>Off</td>
<td>Off</td>
</tr>
<tr>
<td>Glucagon</td>
<td>Off</td>
<td>On</td>
<td>Off</td>
</tr>
<tr>
<td>Insulin</td>
<td>Off</td>
<td>Off</td>
<td>Off</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Off</td>
<td>Off</td>
<td>On</td>
</tr>
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</table>
Remember:
Unlike gametes (egg and sperm cells), all other cells (somatic cells) have the same DNA content and the same genes.

We can account for different protein patterns in different types of cells:

the expression pattern of genes within different types of cells is NOT identical.
All stem cells are not alike!

- Some stem cells have more potential than others. **POTENCY** describes this flexibility.

- **Unipotent** stem cells form only one type of specialized cell type.

- **Multipotent** stem cells can form multiple types of cells and tissue types.

- **Pluripotent** stem cells can form most or all cell types in the adult.

- **Totipotent** stem cells can form all adult cell types as well as the specialized tissues to support development of the embryo (e.g., the placenta)
STEM CELL BASICS

II. Where do stem cells come from?
Different sources of stem cells during development

Adapted from Stem Cells and Cloning by K.A. Hogan
Isolation of Human Embryonic Stem Cells

First done by Dr. James Thompson and colleagues at the University of Wisconsin (1998).
“Scientists Turn Human Skin Cells into Stem Cells”

Induction of Pluripotency: From Mouse to Human

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DOI 10.1016/j.cell.2007.11.020
Adult Stem Cell Research in the News!
Selected News about Adult Stem Cells

“Scientists Find Way to Track Stem Cells in Brain”  
(Science, November 2007)

“Stem Cells Restore Memory in Mice”  
(Journal of Neuroscience, October 2007)

“Researchers Isolate Adult Stem Cells for First Time in Tendon”  
(Nature Medicine, September 2007)

“Stem Cells From Testes Produce Wide Range of Tissue Types”  
(Nature, September 2007)

“First Neurons Created from ALS Patient’s Skin Cells”  
(Science, July 2008 [online])

“Wisconsin team grows retina cells from skin-derived stem cells”  
(PNAS, August 2009 [online])

“Mouse Study: Uterine Stem Cells Used To Treat Diabetes”  
(Molecular Therapy, August 30, 2011)

“Scientists Discover New Class Of Stem Cell-Like Cells In Spinal Cord”  
(PLoS ONE September 12, 2011)
IMPACT:

• Understanding birth defects
• Possibility of generating patient-specific stem cell lines to study the mechanism of different diseases in the laboratory
• Creation of models for drug discovery and testing the toxic effects of drugs
• Tissue engineering (e.g., use of progenitor cells to make artificial bladders, retinas)
• How does this alter the debate about the use of human ES cells or not?
**Parkinson’s Disease (PD): Stem Cell Insights**

<table>
<thead>
<tr>
<th>Source cells</th>
<th>Differentiated Cell type</th>
<th>Host animal receiving brain transplant</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monkey ESCs</td>
<td>Dopamine-producing neurons</td>
<td>Monkey model of PD</td>
<td>Diminished PD symptoms; low survival rate of transplanted cells</td>
</tr>
<tr>
<td>Human ESCs</td>
<td>Dopamine-producing neurons</td>
<td>Rat model of PD</td>
<td>Significantly improved muscle coordination; tumor formation in brains</td>
</tr>
<tr>
<td>Human neural progenitor cells from fetal tissue engineered to express a “survival factor”</td>
<td>N/A</td>
<td>Rat and monkey models of PD</td>
<td>Improved symptoms of PD; new dopamine-producing neurons generated; effects not long lasting</td>
</tr>
<tr>
<td>Adult human brain biopsy cells</td>
<td>Neural progenitor cells</td>
<td>Mouse</td>
<td>New neurons generated</td>
</tr>
<tr>
<td>Mouse or human neural ASCs</td>
<td>N/A</td>
<td>Mouse model of related disease, Sandhoff’s disease</td>
<td>Increased life span; delayed loss of motor function; no tumors</td>
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adapted from K.A. Hogan, *Stem Cells and Cloning.*
Stem Cell Therapy Challenges

• Safety challenges
  Use of ESCs or differentiated cells derived from ESCs for therapy:
    - Considerations to avoid tumor formation.
    - Immune system challenges to avoid rejection of foreign cells.

• Understanding the basic mechanisms that underlie stem cell biology

• Social, ethical, political considerations for ESC research
Ethical Issues surrounding the stem cell debate

Dr. Elaine Fuchs:  (iBioseminars.org)
“Stem Cells: Biology and Promise for Regenerative Medicine”

1) Ethical Issues

2) Alternative methods for producing embryonic stem cells
Summary:

• Stem cell therapies offer regenerative prospects for numerous human diseases

• Stem cells are capable of renewal and differentiation.

• Stem cells are derived from numerous sources and have different potency capacities.

• Adult stem cells (ASCs) have been detected in numerous tissues.

• Considerable ethical debate surrounds the use of embryonic stem cells. Adult stem cells may offer similar prospects for therapy as do ESCs, yet a complete understanding of stem cell applications will require a basic understanding of differentiation and renewal mechanisms in ASCs and ESCs as well.

Additional resources:  http://stemcells.nih.gov/info/basics/ www.stemcellresearchnews.com