Stem Cells: Introduction and Prospects in Medicine (Part I)

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Bioscience in the 21st Century
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Overview

• Setting the stage for the discussion: historical perspective and prospects in regenerative medicine

• Stem Cell Basics:
  – What are stem cells?
  – Where do stem cells come from?

• Stem Cell Therapy Challenges

• Selected Stem Cell Advance in the News:
  Prospects for treating Type 1 Diabetes
Historical Perspective and Prospects for Regenerative Medicine
Historical Perspectives

• Major changes in regenerative medicine (replacement of damaged or diseased cells and tissues with new cells and tissues) 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 believed to have greater potential. This line of stem cell research has been the most controversial.
KEY STEM CELL DEVELOPMENTS

- 1981: discovery of mouse embryonic stem cells (mESC)
- 1998: discovery of human embryonic stem cells (hESC)
- 2006: discovery of human induced pluripotent stem cells (hiPSCs)
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.

2012 Novel Prize in Physiology or Medicine

Sir John B. Gurdon and Shinya Yamanaka for the discovery that mature cells can be reprogrammed to become pluripotent. “

http://www.nobelprize.org/nobel_prizes/lists/year/?year=2012
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)
I. What are stem cells?
Basic Characteristics of Stem Cells

Stem cells properties:
1. Capable of dividing and renewing for long periods
2. They are unspecialized.
3. They give rise to specialized cells.

Adapted from *Stem Cells and Cloning* by Kelly A. Hogan; http://stemcells.nih.gov/info/basics/basics2.asp
How do cells remain self-renewing and unspecialized?

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

SELF-RENEWAL

DIFFERENTIATION
Gene expression patterns are NOT identical within different cell types.

Some genes are expressed in all cells: others are expressed only in specific cell types.

Figure from *Stem Cells and Cloning* by K.A. Hogan
All stem cells are not alike!

• Some stem cells have more potential than others. POTENCY describes the cell’s ability to differentiate into other cell types.

• 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

[P] = pluripotent
[M] = multipotent
[T] = totipotent

Teratomas (benign); Teratocarcinomas (malignant).
Isolation of Human Embryonic Stem Cells

First done by Dr. James Thompson and colleagues at the University of Wisconsin (1998).

Figure from Stem Cells and Cloning by K.A. Hogan
Properties of Human Embryonic Stem Cells in Culture

- **Pluripotent** – able to form any of ~200 different types of cells of the body
- **Self-renewing in vitro** – can propagate or proliferate indefinitely in the undifferentiated state
- **Express** the enzyme telomerase (required to maintain the ends of chromosomes) and Oct4 (a master regulator of ESC pluripotency)
- **Maintain normal chromosome structure and complement** even after long periods in culture (unlike many other tissue culture cell lines)
“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
Embryonic stem cells derived by nuclear transfer of somatic cell nucleus into an enucleated unfertilized egg

http://en.wikipedia.org/wiki/Somatic-cell_nuclear_transfer

http://ns.umich.edu/stemcells/F_030606a.html
Stem Cell Therapy Challenges

• Ethical considerations for ESC research
• 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
Stem Cell Research in the News!
Selected News about 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)
• “Scientists Turn Human Skin Cells into Stem Cells”
  (Science; Cell, November 2007)
• “First Neurons Created from ALS Patient’s Skin Cells”
  (Science, July 2008 [online])
• “Identification of small molecules for human hepatocyte expansion and iPS differentiation”
  (Nature Chemical Biology, June 2013)
• “Photoreceptor precursors derived from three-dimensional embryonic stem cell cultures integrate and mature within adult degenerate retina”
  (Nature Biotechnology, July 2013)
• “Generation of functional human pancreatic beta cells in vitro”
  (Cell, October 2014)
To be continued on Monday, November 10, 2014