## Embryonic vs Adult Stem Cells - Pros & Cons

### Embryonic Stem (ES) Cells

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Pluripotency</strong> - ability to differentiate into any cell type.</td>
<td>• <strong>Unstable</strong> - difficult to control differentiation into specific cell type.</td>
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<tr>
<td>• <strong>Immortal</strong> - one cell can supply endless amounts of cells.</td>
<td>• <strong>Immunogenic</strong> - potential immune-rejection when transplanted into patients.</td>
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<tr>
<td>• <strong>Easily available</strong> - human embryos from fertility clinics.</td>
<td>• <strong>Teratomas</strong> - tumor composed of tissues from 3 embryonic germ layers.</td>
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<td>• <strong>Ethical Controversy</strong> - unethical for those who believes that life begins at conception.</td>
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</table>
Embryonic vs Adult Stem Cells - Pros & Cons

**Adult Stem Cells**

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<td>• Already ‘specialised’ - induction of differentiation into specific cell types will be easier.</td>
<td>• Minimal quantity - number of isolatable cells may be small.</td>
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<tr>
<td>• Plasticity - Recent evidences suggest wider than previously thought ranges of tissue types can be derived.</td>
<td>• Finite life-span - may have limited life-span in culture.</td>
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<td>• No Immune-rejection - if used in autologous transplantations.</td>
<td>• Ageing - stem cells from aged individuals may have higher chance of genetic damage due to ageing.</td>
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<tr>
<td>• No Teratomas - unlike ES cells.</td>
<td>• Immunogenic - potential immune-rejection if donor cells are derived from another individual.</td>
</tr>
<tr>
<td>• No Ethical Controversy - sourced from adult tissues.</td>
<td></td>
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What is a Stem Cell? - **Pluripotency**

1 Cell
(Zygote - fertilised egg)

6,000,000,000 cells
(230 different cell types)
What makes Stem Cells “Stem Cells”?

Characteristics of Embryonic Stem Cells

**Origin**
- Derived from pre-implantation or peri-implantation embryo
- Blastosyst

**Self-Renewal**
- The cells can divide to make copies of themselves for a prolonged period of time without differentiating.

**Pluripotency**
- Embryonic stem cells can give rise to cells from all three embryonic germ layers even after being grown in culture for a long time.

**Differentiation**
- The three germ layers and one example of a cell type derived from each layer:
  - Ectoderm: Nerve cells, skin, hair, teeth, eyes, nose, and mouth, and sensory pigment cells.
  - Mesoderm: Muscles, blood, blood vessels, connective tissue, and the heart.
  - Endoderm: Liver, gut, lungs, bladder, and germ cells (eggs or sperm)

Figure 1.2. Characteristics of Embryonic Stem Cells.
What makes Stem Cells, ‘Stem Cells’?

**Self-Renewal**
through Asymmetric Cell Division

**Differentiation**
via Multipotent Progenitors
Self-Renewal vs Differentiation

Figure 2.1. Hematopoietic and stromal cell differentiation.
Skeletal Muscle Biology

(a) Fusion of myoblasts into muscle fiber

(b) Muscle fiber

Muscle
- Epimysium
- Perimysium
- Fasciculus

Group of muscle fibers
- Sarcolemma
- Myofibril
- Sarcoplasm
- Capillary
- Endomysium
Myogenic Lineage

Paired-box transcription factors
*Pax3, Pax7*

bHLH transcription factors
Myogenic Regulatory Factors (MRFs)
*MyoD, Myf-5, myogenin*

Tajbakhsh *Exp Cell Res* 2005
Myogenic Lineage

- Stem Cell: $\text{Pax}^3+$ and/or $\text{Pax}^7+$
- Proliferation
- Myogenic Specification: $\text{Myf}^5+$, $\text{MyoD}^+$
- Differentiation: $\text{MyoD}^+$, $\text{Myogenin}^+$
- Terminal Differentiation: $\text{Myogenin}^+$, $\text{MHC}^+$

Modified from Tajbakhsh (2003)
Current Opinion in Genetics & Development
Developing Muscles from Rat Hindlimb

Cryostat Section

Isolated Cells

Triple Immuno-labeling;
Pax3+
Pax7+
MRFs+ (MyoD+Myf-5+myogenin)

Pax3+
Pax7+
MRFs+
Pax3+ Pax7+
Pax3+ MRFs+
Pax7+ MRFs+
Pax3+ Pax7+ MRFs+
Adult Muscle Stem (Satellite) Cells
Symmetric vs Asymmetric Division

Symmetric Division

Asymmetric Division

Stem Cell

Differentiated Cell

Self-Renewal
Symmetric vs Asymmetric Division

Stem Cell

- Pax3$^+$
- Pax7$^+$ and/or

Proliferation

- Pax7$^+$

Myogenic Specification

- Myf5$^+$, MyoD$^+$

Differentiation

- MyoD$^+$, Myogenin$^+$

Terminal Differentiation

- Myogenin$^+$, MHC$^+$
Symmetric vs Asymmetric Division

Symmetric division: sister cells become different as result of influences acting on them after their birth.

Asymmetric division: sister cells born different.
Asymmetric Cell Division - Stem Cell Hallmark

Environmental Asymmetry

Divisional Asymmetry

Differentiated Cell

Differentiated Cell
Divisional Asymmetry

A. Extrinsic Regulation

- adding growth factors & cytokines.
- changing surface properties of the culture dish.
- co-culture with ‘feeder’ cells.
- co-culture with scaffolding or matrix.
- activation of transcription factors.

B. Intrinsic Regulation

Engineering the ‘Niche’...

Yamashita Cold Spring Harb Perspect Biol 2010
Cancer Stem Cells?

1. Stem cell
   - Stem cell
   - Normal stem cell
   - Mutated stem cell, or self-renewal genes turned on

2. Progenitor cell
   - Normal progenitor cell
   - Mutated progenitor, or self-renewal genes turned on
   - Loss of regulated cell division
   - Self-renewal genes turned on

3. Differentiated cell
   - De-differentiated cell
   - Cancer stem cell

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UNSW
THE UNIVERSITY OF NEW SOUTH WALES
SYDNEY • AUSTRALIA
1. Generation of cells/tissues for Cell-Based Therapies
Stem Cells - *Therapeutic Applications*

2. Drug discovery/screening through safer and cheaper testing using human cells.
3. Study the mechanisms of human development, stem cell differentiation and function.
4. Study the mechanisms to understand and treat birth abnormalities.
Summary

• Stem Cell Definition?
  • Totipotency - Pluripotency - Multipotency

• Various sources of Stem Cells?
  • Advantages & Disadvantages

• Unique feature of “Stem Cells”?
  • Self-Renewal vs Differentiation and how this could be achieved

• Therapeutic applications of Stem Cells?
  • Find out examples that spark your interests from the news and media for discussion in Lab 12.
Lab 11 - Information & Overview

Please ensure that you read and bring the Laboratory Handout for the Laboratory Session tomorrow.

Questions?