Tissue Engineering: Cells

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Autologous (from same individual)
- Differentiated cells of same or other tissue type
  - Stem cells (e.g., from bone marrow, fat or other tissue, or saved from umbilical cord)

Allogeneic (from another individual)
- Differentiated cells of same or other tissue type
  - Fetal stem cells
  - Embryonic stem cells

Xenogeneic (from another species)
- Same as allogeneic

<table>
<thead>
<tr>
<th>Cells for Tissue Engineering/Regenerative Medicine</th>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Autologous vs. Allogeneic vs. Xenogeneic Cells</td>
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<tr>
<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
<td></td>
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<tr>
<td>Auto</td>
<td>No disease transmission</td>
<td>Donor site morbidity</td>
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<tr>
<td>Allo</td>
<td>Large available pool</td>
<td>Disease transmission</td>
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<td></td>
<td>Less expensive</td>
<td>Immune reaction</td>
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<td></td>
<td></td>
<td>Heterogeneous pop. (genetic anomalies)</td>
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<tr>
<td>Xeno</td>
<td>Largest pool</td>
<td>Disease transmission</td>
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<tr>
<td></td>
<td>Least expensive</td>
<td>Immune reaction</td>
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<tr>
<th>Stem Cells Versus Differentiated Cell Types</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Diff.</td>
<td>Already display the desired phenotype</td>
<td>Donor site morbidity</td>
</tr>
<tr>
<td></td>
<td>More expensive procedure</td>
<td>Difficulties in growth</td>
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<td></td>
<td></td>
<td>in vitro</td>
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<tr>
<td>Stem</td>
<td>Several sources</td>
<td>May not differentiate</td>
</tr>
<tr>
<td></td>
<td>Easier to obtain</td>
<td>as desired</td>
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<tr>
<td></td>
<td>Less expensive</td>
<td>Uncontrolled growth</td>
</tr>
<tr>
<td></td>
<td>Can be used for many applications; undiff. and diff.</td>
<td>and differentiation</td>
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<td>in vivo</td>
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NEED FOR STEM CELLS IN TISSUE ENGINEERING/REGENERATIVE MEDICINE

Problems in Using Differentiated Cells
- Limited availability of differentiated autologous cells.
- Morbidity of a harvest procedure and donor site.
- Limited proliferative capacity and biosynthetic activity.

Can Adult Stem Cells Suffice?
- Stem cells can be found in many tissues of the body and developing embryos and fetuses
  - ES cells are pluripotent: with the correct cues they can give rise to any kind of cell in the body
  - Adult stem cells are multipotent: they can produce many, but not all, cell types
- Adult bone marrow cells have been in use for more than a decade, whereas embryonic stem (ES) cells were isolated for the first time 3 years ago
- Surprising flexibility of adult stem cells found in many tissues
- ES cells multiply more readily and seem far more proficient in producing certain specialized cell types


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Stem Cells: A Primer
Definitions
- Stem cells - cells that have the ability to divide for indefinite periods in culture and to give rise to specialized cells.
  - Multipotent - giving rise to many cell types.
  - Pluripotent - capable of giving rise to most tissues of an organism.
  - Totipotent - having unlimited capability. Totipotent cells have the capacity to specialize into extraembryonic membranes and tissues, the embryo, and all postembryonic tissues and organs.

CELLS BEING REFERRED TO AS “STEM CELLS”
- Can divide in culture for only a limited number of passages and still be induced to differentiate into selected cell types (i.e., cannot divide indefinitely).
- Can only be induced to differentiate into only a few specialized cell types.
- Most tissues appear to contain such cells.
**STEM CELLS FROM MARROW**

**Rationale for Clinical Value**

**Historical Perspective**

1869  Autologous marrow induces bone at heterotopic sites (E. Goujon)

1919  Marrow has osteogenic activity (A. Keith)

1961  Osteogenic properties of marrow (RG Burwell)


1995  Marrow infiltrating into defects in articular cartilage provide stem cells for chondrogenesis

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**MSC Differentiation Assays In Vitro**

- **Hyaline Cartilage**
- **Bone**
- **Fat**
- **Von Kossa**

Chondro-induced adult canine MSCs in a Type II Collagen-GAG matrix after 2 weeks (+100ng/ml of IGF-1)

Safranin O staining