Stem Cell Therapies

Ocular Therapeutics 2020

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Sources of stem cells

- Embryonic Stem Cells
- Fetal Stem Cells
- Infant Stem Cells
- Adult Stem Cells

Potency of Stem Cells

- ESCs: Pluripotent
- iPSCs: Pluripotent
- Adult SCs: Oligopotent

Properties of Stem Cells

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ESCs</th>
<th>iPSCs</th>
<th>Adult SCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferation</td>
<td>Very High</td>
<td>Very High</td>
<td>Limited</td>
</tr>
<tr>
<td>Potency</td>
<td>Pluripotent</td>
<td>Pluripotent</td>
<td>Oligopotent</td>
</tr>
<tr>
<td>Clinical use</td>
<td>Require Induction</td>
<td>Require Induction</td>
<td>Direct transplant</td>
</tr>
<tr>
<td>Tumorogenicity</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ethical issue</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Autologous</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Barriers to Clinic
• Adipose tissue derived stem cells used by “stem cell clinics” in US
• 3 patients presented with severe visual loss after intravitreal injection of autologous adipose stem cells.
• Vision ranged from 20/30 to 20/200 prior to treatment
• 1 year post treatment, vision is 20/200 to light perception

“If it looks like a crook ......”

• Clinic had no research track record
• Patients were charged for treatment
• Both eyes were treated

Stem Cell Therapy Principles

• Research
• Academic led
• Evidence based medicine
• ‘Primum non nocere’

Regenerating the Cornea with Stem Cells

1. Expanded Stem Cells
2. Induced Pluripotent Stem Cells
3. Umbilical Stem Cells

1. Expanded stem cell transplant
**Human Corneal Stem Cells**

- Image of human corneal stem cells.

**Stem Cell Sphere Formation**

- Isolated cells form spheres.
- Spheres label with p63.

**Spheres Produce Corneal Cells**

- Epithelium Cytokeratin 3/12
- Keratocytes Vimentin

**Repopulation of the stroma**

- Spheres implanted in tissue are able to provide cells.
- Which migrate extensively.
Keratoconic Tissue

Spheres Repopulate Keratoconic Stroma

Keratocyte gene expression

2. Induced Pluripotent Stem Cells

Induction of NCCs
Induction of NCCs

AP2a  DAPI + AP2a

iPSC to NCC Transition

neural crest markers  pluripotency markers

Repopulation of the stroma

seeded with iP5-derived NCCs

….. with Keratocytes

neural crest markers  keratocyte markers

3. Umbilical Stem Cells

Cord (UC)  Cornea
Structural similarities –

Epithelium

Mesenchymal stem cells

Keratocytes

Endothelium

Umbilical cord

Cornea

Bowman’s layer

Descemet’s membrane

Wharton’s Jelly

MSC – MESENCHYMAL STROMAL CELLS

Wharton’s Jelly

• MSC – Mesenchymal stromal cells

Droplet digital PCR indicates MSC

Intrastromal injection

MSC Characterisation - flow cytometry

Intrastromal injection
Recellularised cornea with umbilical cells

Barriers to Clinic

Thank you

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