Stem Cell for Spine Care
- From dish to disc

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Disclosures

- Consultant, DePuy Synthes
- Board of Directors, American Academy of Regenerative Medicine
- Board of Directors, Society of Chinese American Physician Entrepreneurs
Goals for Discussion

1. To recognize the activities of stem cells
2. To review stem cells based on strategy of preparation
3. To familiarize with current regen spine service and translational research
Processes of Disc & Cartilage Degeneration

• Three processes
  • Cellular process
    • Apoptosis
  • Molecular process
    • Cytokine profile
    • Matrix degradation
• Painful experience
  • AP frequency ↑

- Aging
- Genetic
- Mechanical Stress
- Obesity
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- Aging
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### Source of MSCs

<table>
<thead>
<tr>
<th>Human tissue source</th>
<th>CFU-F yield (per cc of tissue)</th>
<th>MSC frequency range (CFU-F/10⁶ nucleated cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow aspirate</td>
<td>109–664</td>
<td>10–83</td>
</tr>
<tr>
<td>Adipose/lipoaspirate</td>
<td>2058–9650</td>
<td>205–51000</td>
</tr>
<tr>
<td>Umbilical cord blood</td>
<td>0.06</td>
<td>0–0.02</td>
</tr>
<tr>
<td>Synovial fluid</td>
<td>4–14</td>
<td>2–250</td>
</tr>
<tr>
<td>Amniotic fluid</td>
<td>3</td>
<td>9.2</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>0</td>
<td>0-2</td>
</tr>
<tr>
<td>Dermis</td>
<td>Not reported</td>
<td>74 000– 157000</td>
</tr>
</tbody>
</table>

Murphy, *Experimental & molecular medicine*, 45(11), e54.
Five Generations of Stem Cells Based on Preparation Strategy

**Sources**
- Bone marrow
- Adipose tissue
- Umbilical cord
- iPS cells

**Preparation**
- MSCs procured with minimal manipulation (G1)
- Culture expanded MSCs (G2)
- Lineage-directed or preconditioned MSCs (G3)
- Genetically modified SCs (G4)

**Stem cells transplanted**

Hunt, 2017
Five Generations of Stem Cells Based on Preparation Strategy

Sources
- Bone marrow
- Adipose tissue
- Umbilical cord
- iPS cells (G5)

Preparation
- MSCs procured with minimal manipulation (G1)
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- Stem cells transplanted
Technique of Bone Marrow Aspiration
Current Regen Pain Services

- Bone Marrow Aspirate Concentrate Injection

Bone Marrow Aspiration

Bone Marrow Aspirate Concentrate (BMAC)

Bone Marrow Mesenchymal Stem Cell (BMSC)

BMAC Injection
- Disc
- Facet
- SIJ
## G1: Bone Marrow Aspirate Concentrate

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Design</th>
<th>N</th>
<th>Indication</th>
<th>Outcomes</th>
<th>AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pettine et al 2015</td>
<td>Prospective Open label</td>
<td>26</td>
<td>IVD</td>
<td>ODI 57-&gt;24** VAS 79-&gt;33** MRI</td>
<td>None</td>
</tr>
<tr>
<td>Pascual-Garrido et al 2012</td>
<td>Prospective Open label</td>
<td>8</td>
<td>Chronic patellar tendinopathy</td>
<td>Lysholm Tegner2-&gt;8* Cincinnati, IKDC 36-&gt;69* KOOS 44-&gt;71* diagnostic US</td>
<td>None reported</td>
</tr>
<tr>
<td>Yan et al, 2015</td>
<td>Retrospective Decom vs Decom+ BMAC</td>
<td>86 (42 vs 44)</td>
<td>Femoral head AVN</td>
<td>VAS both* w/ trend</td>
<td>None</td>
</tr>
<tr>
<td>Shapiro et al, 2016</td>
<td>RCT BMAC vs Saline</td>
<td>25</td>
<td>Knee OA</td>
<td>VAS both* No grp diff</td>
<td>None</td>
</tr>
</tbody>
</table>
Five Generations of Stem Cells Based on Preparation Strategy

Sources

- Bone marrow
- Adipose tissue
- Umbilical cord
- iPSC cells (G5)

Preparation

MSCs procured with minimal manipulation (G1)

Culture expanded MSCs (G2)

Lineage-directed or preconditioned MSCs (G3)

Genetically modified SCs (G4)

Stem cells transplanted
Transform the Practice Initiative Trial
- AMSCs for discogenic pain
- Culture Expanded AMSC Injection

Adipose Biopsy

Adipose Derived Mesenchymal Stem Cell (BMSC)

Culture Expansion of AMSC

AMAC Injection
- Intradiscal
- Therapy Arm
Industry Trial for Discogenic Pain

- Culture Expanded BMSC Injection

Bone Marrow Aspiration → Bone Marrow Mesenchymal Stem Cell (BMSC) → Culture Expansion of BMSC → BMAC Injection

- Intradiscal Therapy Arm
- Control Arm
# G2: Completed Trials on Discogenic Pain

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Design</th>
<th>Cell type</th>
<th>Dosage</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bae et al. 2014</td>
<td>100</td>
<td>RCT, 3 arms</td>
<td>Allogeneic MPC, immunoselected</td>
<td>6M 18M + HA carrier</td>
<td>VAS, ODI, SF-36, WPAI</td>
</tr>
<tr>
<td>Coric et al. 2013</td>
<td>15</td>
<td>Open label, single arm</td>
<td>Allogeneic chondrocytes, cultured</td>
<td>100-200M with fibrin carrier</td>
<td>NRS, ODI, SF-36, MRI</td>
</tr>
<tr>
<td>Orozco et al. 2011</td>
<td>10</td>
<td>Open label, single arm</td>
<td>Autologous BMSC, cultured</td>
<td>18-28M</td>
<td>VAS, ODI, SF-36, MRI</td>
</tr>
<tr>
<td>Pang et al. 2014</td>
<td>2</td>
<td>Case study</td>
<td>Allogeneic HUC-MSCs, cultured</td>
<td>100M</td>
<td>VAS, ODI, MRI</td>
</tr>
<tr>
<td>Pettine et al. 2016</td>
<td>26</td>
<td>Open label, 2 arms</td>
<td>Autologous BMSC</td>
<td>2-3 ml</td>
<td>VAS, ODI, MRI</td>
</tr>
<tr>
<td>Pettine 2012</td>
<td>14</td>
<td>Open label, single arm</td>
<td>Allogeneic chondrocytes</td>
<td>10M with fibrinogen and thrombin carrier</td>
<td>NRS, ODI, SF-36, MRI</td>
</tr>
</tbody>
</table>
# G2: On-going Trials for Discogenic Pain

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>N</th>
<th>Phase</th>
<th>Design</th>
<th>Cell type</th>
<th>Dosage</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red de Terapia Celular</td>
<td>24</td>
<td>I-II</td>
<td>RCT, 2 arms</td>
<td>Allogeneic BMSC, cultured</td>
<td>25M</td>
<td>VAS, ODI, SF-12, MRI, AEs</td>
</tr>
<tr>
<td>Mesoblast</td>
<td>330</td>
<td>III</td>
<td>RCT, 3 arms</td>
<td>Allogeneic MPC</td>
<td>6M 6M + HA</td>
<td>VAS, ODI</td>
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<tr>
<td>Bioheart</td>
<td>100</td>
<td>II</td>
<td>Open label, single arm</td>
<td>Autologous AMSC + PRP</td>
<td>Will vary</td>
<td>VAS, ODI</td>
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<tr>
<td>Biostar</td>
<td>8</td>
<td>I-II</td>
<td>Open label, single arm</td>
<td>Autologous AMSC</td>
<td>40M</td>
<td>VAS, MRI, AEs</td>
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<tr>
<td>Inbo Han, CHA University</td>
<td>10</td>
<td>I</td>
<td>Open label, single arm</td>
<td>Autologous AMSC</td>
<td>20-40M + HA</td>
<td>VAS, ODI, SF-36, MRI, DHI, AEs</td>
</tr>
</tbody>
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Stem cells transplanted
# State of Stem Cell in Spine Care

<table>
<thead>
<tr>
<th>Generation</th>
<th>Source</th>
<th>Human</th>
<th>Animal</th>
<th>Bench</th>
<th>MSC</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Concentrate</td>
</tr>
<tr>
<td>1st Gen</td>
<td>Auto</td>
<td>√</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>2nd Gen</td>
<td>Auto</td>
<td>√</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Allo</td>
<td></td>
<td></td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>3rd Gen</td>
<td>Auto</td>
<td>√</td>
<td></td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Allo</td>
<td>√</td>
<td></td>
<td>√</td>
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<tr>
<td>4th Gen</td>
<td>Auto</td>
<td>√</td>
<td></td>
<td>√</td>
<td>√</td>
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<tr>
<td></td>
<td>Allo</td>
<td>√</td>
<td></td>
<td>√</td>
<td>√</td>
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<tr>
<td>5th Gen</td>
<td>iPSC</td>
<td>-</td>
<td></td>
<td>-</td>
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</tbody>
</table>
Thank you!
qu.wenchun@gmail.edu