ACELLULAR STEM CELL DERIVATIVES FOR THE TREATMENT OF MUSCLE INJURIES: A NEW PARADIGM?

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<tr>
<th>Name</th>
<th>Disclosures</th>
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Introduction: Acellular Stem Cell Derivatives (ASCD)

Exosomes secreted by progenitor cells containing:

- mRNA, miRNA, IL-10
- Anti-inflammatory
- Fibrinolytic
- Anti-fibrogenic

Beneficial Effects of ASCD in Muscle Tissue Healing:
**LIMITED EVIDENCE**
Purpose and Hypothesis

- **Purpose**: to evaluate the effect of local ASCD administration in the healing process of muscle injuries.

- **Hypothesis**: ASCD *favors* muscle *healing*, because it *decreases* fibrotic tissue formation.
Methods

- Experimental in-vivo muscle traumatic injury
- Animal model (Ethics committee approval)
  - 52 mice, C57 male
- Intervention:
  - ASCD → Human Bone Marrow donors
- Statistical Analysis:
  - Power: 80% / ANOVA (DUN) / p < 0.05
Methods: Study Groups

Mice C57
N = 52

Group 1:
Control: α-MEM (50ul)
n = 10

Day 0
n = 5
Day 14
n = 5

Group 2:
ASCD Low Dose (10ul)
n = 14

Day 0
n = 7
Day 14
n = 7

Group 3:
ASCD Medium Dose (25ul)
n = 14

Day 0
n = 7
Day 14
n = 7

Group 4:
ASCD High Dose (50ul)
n = 14

Day 0
n = 7
Day 14
n = 7

Group 5: Healthy Control (n=52): Left Quadriceps (not intervened)
**Results: Macroscopic Analysis:**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Intervened Control: α-Mem Acute</th>
<th>ASCD High Dose Acute</th>
<th>ASCD High Dose Delayed</th>
<th>Healthy Control</th>
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<tr>
<td>Mass</td>
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<tr>
<td>Atrophy</td>
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<td>Fibrotic Scar</td>
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* Significant Difference vs ASCD High Dose Delayed Group

* Significant Difference vs Healthy Control Group
Results: Histological Analysis

Intervened Control (α-Mem)  ASCD High Dose Delayed  Healthy Control

Fibrosis ↓  p = 0.0004
Discussion

1. Timing of intervention: Why is Delayed ASCD inoculation better?
   - Fibrotic modulation starts at 14 days of injury (Murine)
     - ASCD → Fibrinolytic and Antifibrogenic properties

2. Literature Comparison: Only 1 study (Nakamura et al):
   - Similar results → ASCD promotes muscle healing:
     - Less fibrosis
     - Higher regenerative tissue
   - Differences with our study:
     - Follow up: 5 days (vs 28 days)
     - Chemical injury (vs traumatic injury)
Discussion: **Strengths**

- First study in vivo to assess ASCD in muscle healing using a traumatic muscle injury model.
- Complete (section) muscle injury and Reproducible model:
- Found a biological potential in a commonly discarded resource.
Discussion: Limitations

- No blind observer on macroscopic analysis
  - Agreement with histologic results

- Single evaluation of each sample
  - Consecutive studies have confirmed our results
Conclusion

- 1st In-vivo traumatic muscle injury animal model: Local administration

  **ASCD High Dose**
  **Delayed (14 days)**

  Muscle healing

  Less muscle atrophy and fibrotic tissue

  No difference in mass and volume with healthy controls
References