4-29-2015

Adipose Tissue Therapeutics for Scar Rehabilitation after Thermal Injury

Dylan Perry  
*University of Massachusetts Medical School*

Jorge R. Lujan-Hernandez  
*University of Massachusetts Medical School*

Ava Chappell  
*University of Massachusetts Medical School*

*See next page for additional authors*

Follow this and additional works at: [https://escholarship.umassmed.edu/ssp](https://escholarship.umassmed.edu/ssp)

Part of the Pathological Conditions, Signs and Symptoms Commons, Plastic Surgery Commons, Skin and Connective Tissue Diseases Commons, Therapeutics Commons, and the Tissues Commons

Repository Citation

Perry, Dylan; Lujan-Hernandez, Jorge R.; Chappell, Ava; Min, So Yun; Appasani, Raghu; Rojas-Rodriguez, Raziel; Chin, Michael S.; Corvera, Silvia; and Lalikos, Janice F., "Adipose Tissue Therapeutics for Scar Rehabilitation after Thermal Injury" (2015). University of Massachusetts Medical School. Senior Scholars Program. Paper 191.  
[https://escholarship.umassmed.edu/ssp/191](https://escholarship.umassmed.edu/ssp/191)

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in Senior Scholars Program by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Adipose Tissue Therapeutics for Scar Rehabilitation after Thermal Injury

Authors
Dylan Perry, Jorge R. Lujan-Hernandez, Ava Chappell, So Yun Min, Raghu Appasani, Raziel Rojas-Rodriguez, Michael S. Chin, Silvia Corvera, and Janice F. Lalikos

Keywords
burn injuries, healing, thermal scars, scar remodeling, adipose derived stem cells (ADSCs), lipoaspirate

Comments
Poster presented on Senior Scholars Presentation Day at the University of Massachusetts Medical School, Worcester, MA, on April 29, 2015. Medical student Dylan Perry participated in this study as part of the Senior Scholars research program at the University of Massachusetts Medical School.

Rights and Permissions
Copyright is held by the authors, with all rights reserved.

This poster is available at eScholarship@UMMS: https://escholarship.umassmed.edu/ssp/191
Introduction

THE PROBLEM

- Burn injuries are common and always lead to scarring, especially pathological.
- Molecular analysis of scar remodeling targets such as the wound area.
- Autologous adipose tissue grafting (“Fat Grafting”) and adipose-derived stem cell (ADSC) therapy may improve wound healing and scar outcomes in acute burn, excisional, and radiation skin injury models.
- Clinical case reports suggest adipose therapeutics may improve the remodeling of chronically scarred skin tissue by improving skin color, texture, pliability, and patient symptoms. At least one clinical trial is ongoing.
- Most basic research focuses on acute phase intervention, few if any studies examine adipose derived therapies for improved remodeling of chronic scars.

A POTENTIAL SOLUTION

- Autologous adipose tissue grafting (“Fat Grafting”) and adipose-derived stem cell (ADSC) therapy may improve wound healing and scar outcomes in acute burn, excisional, and radiation skin injury models.
- Clinical case reports suggest adipose therapeutics may improve the remodeling of chronically scarred skin tissue by improving skin color, texture, pliability, and patient symptoms. At least one clinical trial is ongoing.
- Most basic research focuses on acute phase intervention, few if any studies examine adipose derived therapies for improved remodeling of chronic scars.

PROJECT GOALS

- Determine if adipose tissue can improve scar remodeling subacutely after acute wound healing phases have concluded in a mouse model of thermal injury.
- Compare the effects of processed lipos aspirate to adipose derived stem cells.

Materials & Methods

- N = 50 CD1 Nu/Nu (Athymic, nude) mice received standardized 70°C 10s burn (under anesthesia and analgesia) with a brass rod to dorsal skin and monitored for six weeks while chronic scars formed (Fig 1-3).
- At six weeks animals were randomized to five groups (Table 1): non-injected controls received no injection, other groups received subcutaneous injection of 0.6 mL human lipos aspirate, human ADSCs in matrigel hydrogel suspension, or matrigel control. Adipose tissue from discarded human punch. ADSCs from SVF ex-vivo culture.
- Skin perfusion measured with Hyperspectral Imaging (HSI) and digital photos were taken at 4 time points.
- Mice were sacrificed at 10 weeks post-burn (PB) (4 weeks after engraftment) for skin histology.
- Scar wound area and oxy and deoxy hemoglobin (HSI measures) were determined at all time points.
- Skin tissue samples were stained for vascularity (CD31) and collagen composition (Picro-Sirius red, Masson’s Trichrome). Matrigel explants were H&E stained.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Non-injected Control</td>
<td>N=10</td>
</tr>
<tr>
<td>Group 2</td>
<td>Matrigel Control</td>
<td>N=10</td>
</tr>
<tr>
<td>Group 3</td>
<td>Human high density Lipos aspirate</td>
<td>N=10</td>
</tr>
<tr>
<td>Group 4</td>
<td>Low Dose (10^6) ADSCs in Matrigel</td>
<td>N=10</td>
</tr>
<tr>
<td>Group 5</td>
<td>High Dose (10^6) ADSCs in Matrigel</td>
<td>N=10</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Data Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEEK 0</td>
<td>Burn Injury</td>
</tr>
<tr>
<td>WEEK 0.6</td>
<td>Healing Scarring</td>
</tr>
<tr>
<td>WEEK 6</td>
<td>Tissue Harvest</td>
</tr>
<tr>
<td>WEEK 8</td>
<td>Treatment Injection</td>
</tr>
<tr>
<td>WEEK 10</td>
<td>Harvest</td>
</tr>
</tbody>
</table>

Timeline

- Burn Injury
- Healing Scarring
- Treatment Injection
- Tissue Harvest

Results

-Scar wound area: Lipos aspirate treated mice had significantly reduced perceived scar area compared to controls at 10 weeks (Fig 4).
- Histology: CD31 IH trouble. Dermal vessels visualized on Masson’s Trichrome counted in 3 hps/slide show increase in G3 compared to G1 (Fig 5). Collagen microphotomorphometry ongoing. H&E stain of matrigel explants show living cells within hydrogel matrix.
- Hyperspectral imaging: Changes in oxy, deoxy, and total hemoglobin (Hb) consistent all mice until week 6 prior to treatment (not shown). G3 significantly increased oxy Hb from week 6 to 10 compared to other groups (Fig 6). G3-5 significantly lower deoxy Hb compared to G1 10.6 wks (~9.0, not shown). Total Hb reduced (~9.0) in G4-5 compared to G1 at 10.6 wks (not shown).
- ADSC FACs analysis: CD34-, CD45-, CD24-, CD144-, CD90-, CD44+, CD29+. CD73 and CD105 mostly - (fits MSC phenotype).

Future Directions

- Molecular analysis of scar remodeling targets such as TGF-β1/3, α-SMA, col1/3, VEGF, MMP9, SMAD-3.
- Experiment with other hydrogels or no hydrogel in this case: a factor in reducing ADSC efficacy.
- Continue attempts at improving photomorphometric analysis of picro-sirius red collagen staining.
- Include a “supercharged” lipos aspirate group for comparison (Lipo + ADSCs).
- Consider porcine studies, a higher fidelity human skin model and better model of hypertrophic scarring.
- Consider consultation with dermatopathology experts for new clues for histological analysis.

Conclusions

- Lipoaspirate may improve scar remodeling, possibly mediated by increased blood vessel density and improving oxygenation, resulting in smaller perceived scar area.
- Lipoaspirate may retain a native scaffold allowing improved cell survival and angiogenesis preferentially to de novo vasculogenesis from direct ADSC differentiation.
- ADSCs, although promising in other studies, did not improve scar area, perfusion, or BV density in this model. Matrigel may have contributed to this finding as growth factor penetration to healing site may be limited.
- Limitations: Variability in mouse skin phenotype may have contributed error. Burn models are difficult to standardize: burn injury may not have been equal across all mice. Time and resources limited extent of analysis.

References


Contact Info:
Dylan Perry
Medical Student, MS4
Division of Plastic Surgery
Dylan.Perry@UMassMed.edu