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Dylan Perry
*University of Massachusetts Medical School*

*Et al.*

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Adipose tissue therapeutics for scar rehabilitation after thermal injury

Dylan Perry, ¹ Jorge Lujan-Hernandez M.D.,¹ Ava Chappell,¹ So Yun Min,² Raghu Appasani,¹ Raziel Rojas-Rodriguez,² Michael Chin M.D.,³ Silvia Corvera M.D.,² Janice Lalikos M.D.¹

¹Division of Plastic and Reconstructive Surgery. ²Program in Molecular Medicine. ³Division of Radiation Oncology. University of Massachusetts Medical School

Introduction

THE PROBLEM

• Burn injuries are common and always lead to scarring. Deep burns and those taking longer to heal often heal pathologically.

• Scarring, especially pathological hypertrophic scarring, leads to morbid symptoms (pain, pruritus), functional impairment, and negative aesthetic and psychiatric consequences.

• Traditional treatment is excision and skin grafting, a large operation with donor site morbidity and is problematic in complex anatomical areas (face, hands). Other treatment modalities (lasers, silicone, steroids) have side effects, low effectiveness, or lack of supporting evidence.

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 therapeutics 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 lipoaspirate 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 lipoaspirate, human ADSCs or Matrigel hydrogel suspension, or Matrigel control. Adipose tissue from discarded human pannus. 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.

Results

Wound area all groups to 6 weeks (% of original, mean +/- SD)

Vessels per hpf on Masson’s Trichrome (mean +/- SD)

Conclusions

• Lipoaspirate may improve scar remodeling, possibly mediated by increased blood vessel density 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.

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 this was a factor in reducing ADSC efficacy.

• Continue attempts at improving photomorphometric analysis of picrosirius red collagen staining.

• Include a “supercharged” lipoaspirate 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.

References


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