Understanding Kinetics of Rapidly Vascularizing Composite Collagen Dermal Templates (CCDT)

D. Luong[1], R. Cohen,[1] A Weisel[1], Ravyn Dorleus[1], J Yao[3] , J.A. Spector[2], Y. Sapir-Lekhovitser[1]

1] FesariusTherapeutics, Inc.; 2] Weill Cornell Medicine, New York 3] Schweiger Dermatology, New York

Fesarius Therapeutics

Introduction

Reconstitution of skin anatomy following full-thickness skin loss can be achieved using dermal regeneration templates (DRTs) in combination with split-thickness skin grafts (STSGs). However, due to the limited rate of cellular infiltration and vascularization of currently available DRTs, reconstruction typically involves a two-step procedure spaced over several weeks. Our group previously demonstrated that a composite collagen dermal template (CCDT) consisting of a collagen-based 3D structure with a microarchitecture maximizing differential density promotes enhanced cell and vascular invasion, and that a CCDT of 1.5 mm thickness could be placed with a STSG, resulting in a healed wound with reconstituted neodermal layer in a single-step procedure. Here, a follow-up study explores the underlying mechanisms behind these observations.

Methods

CCDTs were prepared using established protocols. Female Yucatan pigs received 3x3 cm full-thickness skin wounds on their dorsum. Wounds were treated with either CCDT or a market-leading DRT (L-DRT), followed by application of standard dressings. Healing was assessed at three time points (3-, 7-, and 10-days post-wound creation). Wounds (N=5/group/timepoint) were harvested and analyzed.

Tissue Deposition

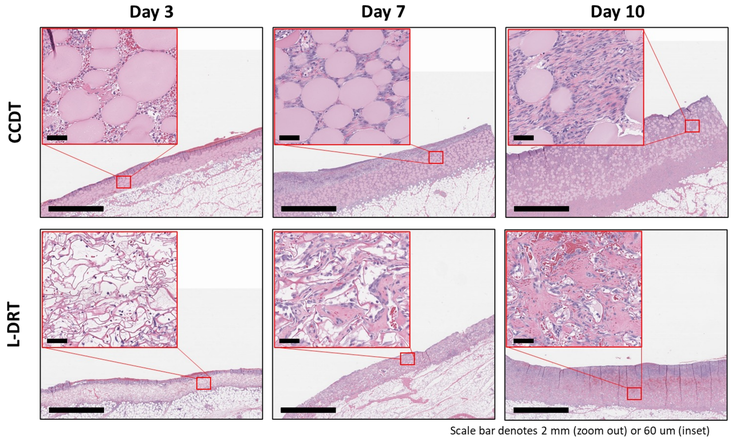

Fig. 1A) H&E staining of hDRT and MLS wounds at day 3-, 7-, and 10-days post implantation.

Cell invasion and "dermal" thickness

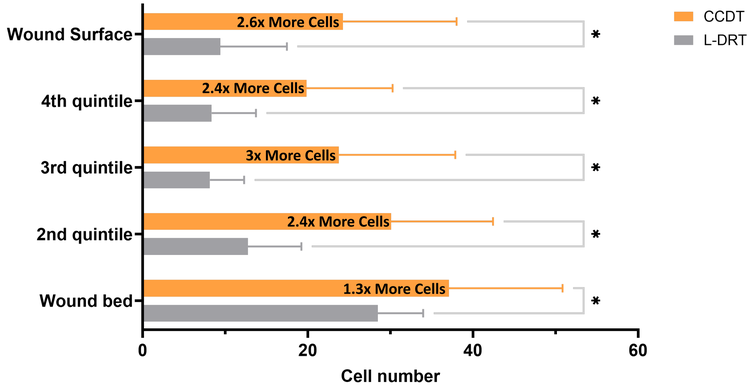

Fig. 1B) Cell counts on day 3 post-implantation for CCDT versus L-DRT, analyzed from the 1st quintile (closest to the wound bed) to the 5th quintile (top of the template). CCDT had consistently higher cell invasion than L-DRT at all quintiles, suggesting enhanced cell permeability at 3 days post-implantation.

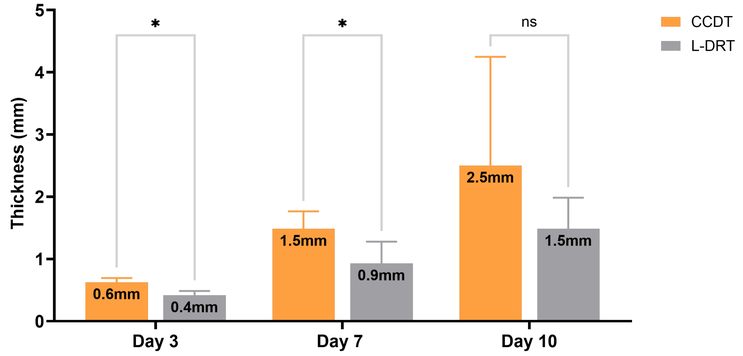

Fig. 1C) Comparison of dermal thickness: CCDT vs. L-DRT at days 3, 7, and 10. CCDT had significantly higher dermal thickness at days 3 and 7 but not day 10, suggesting that CCDT enhances tissue deposition at earlier timepoints.

Financial Disclosure:
1. Employees of and maintain stock options in FesariusTherapeutics, Inc.
2. Founding shareholder and Chief Medical Officer of FesariusTherapeutics, Inc.

Neovascularization

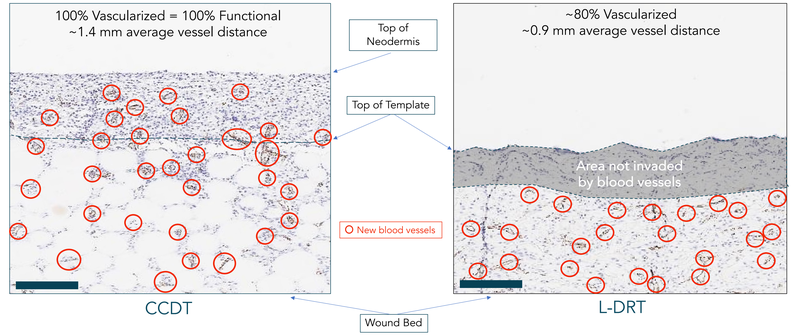

Fig. 1D) CD31 staining of CCDT and L-DRT at 7 days post-implantation. Red circles denote luminal structures indicating blood vessels. At this timepoint, CCDT scaffolds were fully infiltrated by vascular structures throughout their entire thickness and extended into the tissue above the scaffold. In contrast, L-DRT scaffolds were also infiltrated by blood vessels but did not achieve complete penetration through the scaffold's entire thickness.

Results

- CCDT-treated wounds showed 100% engraftment efficiency (5/5 templates fully taken at explantation) by day 3, compared to 0% (0/5 templates fully taken at explantation) in the L-DRT group
- CCDT demonstrated superior cellular invasion on day 3 **(Fig. 1B)**
- CCDT templates presented clear evidence of CD31+ cells by day 3, while L-DRT templates had sparse CD31+ cells
- CCDT-treated wounds had significantly greater dermal thickness on days 3 and 7 **(Fig. 1C)**
- CCDT templates were fully vascularized by day 7, while L-DRT was not **(Fig. 1D)**

Conclusion

These findings suggest that CCDT facilitates faster, more effective cellular invasion and vascularization of the template, leading to early, reliable deposition of functional neodermal tissue, outperforming the L-DRT. This establishes a clear paradigm for previous studies, supporting CCDT's efficacy in single stage grafting procedures.