The Role of Endogenously Expressed IL-10 in Wound Closure and Tissue Repair

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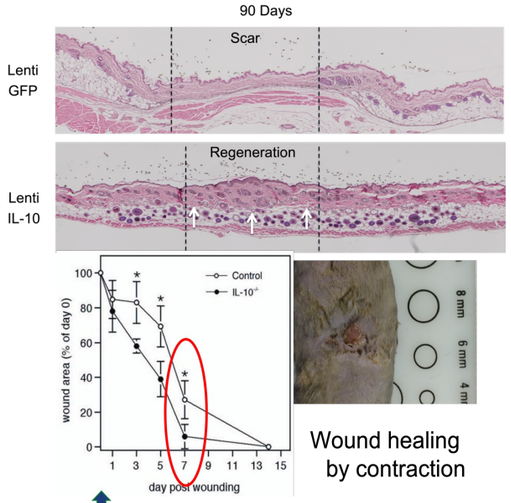
BACKGROUND

IL-10 → Regenerative Wound Healing



Wound healing by contraction

Wound closure rate in IL-10$^{-/-}$ mice

- Our lab has shown a significant role for IL-10 overexpression in regulating inflammation and attenuating fibrosis in skin wounds [1,2].
- A previous study reported increased rate of dermal wound closure in IL-10$^{-/-}$ mice, suggesting IL-10 delays wound healing [3]. However, these studies did not control for contraction in murine skin and a moist wound environment in their models.

PURPOSE

- **The objective of this study** is to determine how IL-10 affects wound closure in a contraction and moisture controlled wound environment using murine full thickness excisional wounds.

RESULTS

Stenting prolongs epithelial gap closure, and wounds in WT and IL-10$^{-/-}$ mice heal at similar rates and α-SMA and when stented

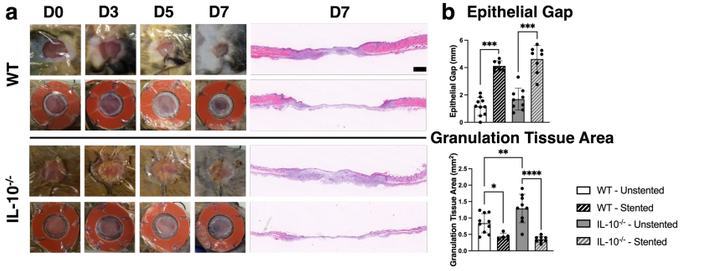


Fig 1: Healing progression of unstented and stented wounds in WT vs IL-10$^{-/-}$ mice at 7 days post-wounding. Stenting slowed wound closure and healing, leading to increased epithelial gap and lower levels of granulation tissue area at day 7. IL10$^{-/-}$ wounds maintained in a moist wound environment showed no significant difference in epithelial gap at D7, but an increase in granulation tissue area compared to WT.

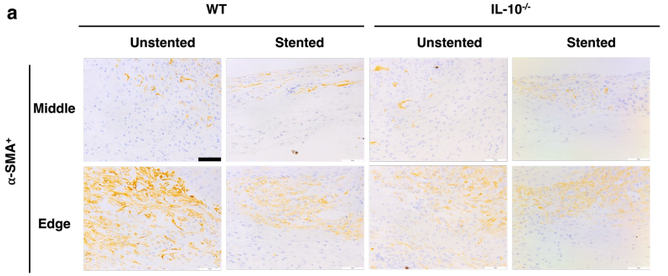


Fig 2: αSMA immunohistochemical staining of unstented and stented wounds in WT vs IL-10$^{-/-}$ mice at 7 days post-wounding. αSMA staining showed abundant expression at the wound margins in all wounds, but stented wounds had more αSMA present in the granulation tissue compared to unstented wounds. IL-10$^{-/-}$ wounds had more αSMA staining in the wound bed than WT. However, analysis of the % of αSMA + cells/HPF showed no significant difference in the stented and unstented wounds.

Stenting alters the inflammatory infiltration in the healing wound

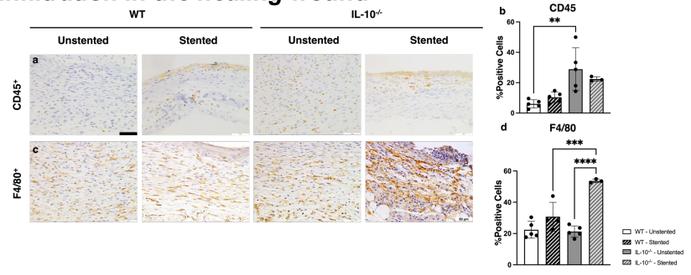


Fig 3: CD45 and F4/80 immunohistochemical staining of unstented and stented wounds in WT vs IL-10$^{-/-}$ mice at 7 days post-wounding. There was a significantly higher percentage of CD45+ cells per HPF in unstented IL10$^{-/-}$ mice compared to unstented WT mice. IL-10$^{-/-}$ mice had a significantly higher % of macrophages per HPF when stented as compared to WT and unstented IL-10$^{-/-}$ wounds.

Loss of IL-10 expression results in greater dermal fibrosis

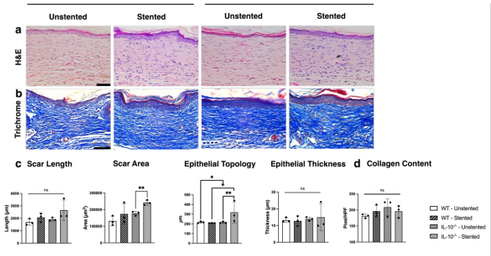
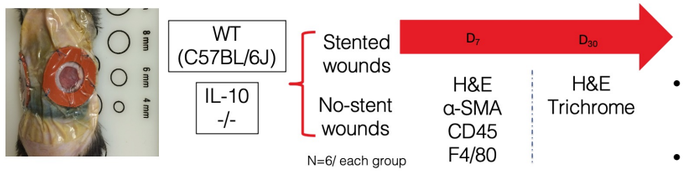


Fig 4: : H&E and Trichrome staining of unstented and stented wounds in WT vs IL-10$^{-/-}$ mice at 30 days post-wounding. The stented IL10$^{-/-}$ group had significantly greater scar area than the unstented IL10$^{-/-}$. There was also a significantly higher measure of epithelial topology in the IL10$^{-/-}$ stented cohort than in the WT stented and IL10$^{-/-}$ unstented groups. We also noted dense collagen bundles in the dermis of both stented and unstented wounds of the IL-10$^{-/-}$ mice as compared to their WT counterparts. However, this trend was not statistically significant.

METHODS



- Full thickness 6mm bilateral wounds were made and a moist wound environment was maintained by Tegaderm.
- Wounds were serially photographed at 3, 5 and 7d.
- Wounds were harvested at 7d and 30d post wounding.
- 7d wounds were analyzed using H&E, α-SMA, CD45, and F4/80.
- 30d wounds were stained with H&E and Trichrome.
- Data: mean±SD, n=8-10 wounds/group/time point; p-value by ANOVA.

CONCLUSIONS

- IL-10 expression does not delay normal wound healing of skin wounds when controlled for contraction and moist environment.
- However, the loss of IL-10 leads to increased inflammation and fibrosis. This data signifies a previously unrecognized role for endogenously expressed IL-10 contributing to the tissue repair response in dermal wounds.

REFERENCES

1. Balaji et al. FASEB 2017 p.868-881
2. Short et al. Annals of Surgery 2021p. 627-636
3. Eming et al. AJP 2007 p.188-202