THE ORAL MUCOSA IS ENRICHED WITH INFLAMMATORY FIBROBLASTS IN DIABETIC MICE
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Introduction
The wound healing process is initiated when tissue is damaged. This dynamic process involves activation of various stromal cells, such as fibroblasts, in the wound site. Recently, studies have suggested that proinflammatory fibroblasts play a critical role in releasing cytokines that recruit immune cells to injury sites and chemokines like CXCL12. Systemic conditions like diabetes mellitus can impair the wound healing process. In this study, we aim to identify the inflammatory fibroblast phenotype in wounded oral mucosa of diabetic mice.

Materials and Methods

Results

There is impaired oral mucosal wound healing in diabetic mice in comparison to normoglycemic (NG) mice. Although there are no significant differences in wound gaps, there was a higher frequency of open wounds in diabetic mice. Collagen deposition was impaired in diabetic mice with an 8% reduction compared to normoglycemic counterpart (p=0.05). Additionally, scRNA-seq analysis revealed higher expression of CXCL12 in diabetic fibroblasts, which was confirmed by RNAscope analysis using the CXCL12 and PDGF receptor alpha marker (p=0.0655) which targets fibroblasts.

Discussion and Conclusion

Our results display an enrichment of CXCL12+ fibroblasts and reduced collagen deposition in the connective tissue of diabetic compared to normoglycemic mice.

Several chronic inflammatory diseases have reported an inflammatory fibroblast subtype in inflamed tissues. This population subtype is enriched in the CXCL1-chemokine family namely CXCL1 and CXCL12. Functionally, inflammatory fibroblasts can recruit granulocytes. Our results are in line with proinflammatory fibroblast phenotype description as we found an increase in CXCL5, CXCL12 and CXCL1 in diabetic mice. Future research should address mechanisms dictating CXCL12+ fibroblast cell fate in diabetic conditions, its impact on other cell recruitment, and shed light on treatments to rescue the diminished collagen production.

References

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