## Fibroblast

A fibroblast is a type of cell that synthesizes the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and plays a critical role in wound healing. Fibroblasts are the most common cells of connective tissue in animals.

The proliferative cells are the fibroblasts near the spinal muscle tissues. The pathological scar will develop to hypertrophy capsule and form membranous tissue after laminectomy. This phenomenon was found by LaRocca and Macnob in 1974<sup>1)</sup>.

Dermal fibroblasts are cells within the dermis layer of skin which are responsible for generating connective tissue and allowing the skin to recover from injury.

Using organelles (particularly the rough endoplasmic reticulum), dermal fibroblasts generate and maintain the connective tissue which unites separate cell layers.

Furthermore, these dermal fibroblasts produce the protein molecules including laminin and fibronectin which comprise the extracellular matrix. By creating the extracellular matrix between the dermis and epidermis, fibroblasts allow the epithelial cells of the epidermis to affix the matrix, thereby allowing the epidermal cells to effectively join together to form the top layer of the skin.

## Growth

Fibroblast growth factor

## Subpopulations

Despite various treatment options available, keloid treatment remains a major clinical challenge due to high recurrence rates and inconsistent therapeutic outcomes. By collecting three keloid tissues and three normal skin samples and utilizing single-cell RNA sequencing (scRNA-seq), Zhao et al. delved into the cellular heterogeneity and molecular mechanisms of keloids. The study identified multiple fibroblast subpopulations within keloid tissue. Enrichment and cell-cell communication analyses revealed that POSTN-positive mesenchymal fibroblasts (POSTN+ mesenchymal fibs) are more prevalent in keloids and exhibit higher transforming growth factor  $\beta$  (TGF- $\beta$ ) signaling activity, potentially playing a central role in excessive fibrosis. In contrast, IGFBP2-positive fibroblasts (IGFBP2+ fibs) are more abundant in normal skin, insensitive to TGF-β and Periostin signaling, and possess anti-fibrotic potential, possibly related to limited tissue repair and regenerative capacity. Trajectory analysis inferred the differentiation states and patterns of different fibroblast subpopulations. Additionally, they explored the heterogeneity of endothelial cells, finding an endothelial cell subpopulation (EC10) exhibiting mesenchymal activation characteristics, which may work with specific fibroblasts to promote abnormal angiogenesis and endothelial-to-mesenchymal transition processes. Spatial transcriptomics analysis has shown that the proportion of IGFBP2+ fibroblasts relatively increases in acne keloidalis after hormonal treatment, further demonstrating their value as potential therapeutic targets. Ultimately, they separated these two subpopulations using flow cytometry, highlighting their opposing roles in the secretion of the ECM. These findings

provide new insights into the pathogenesis of keloids and lay the theoretical foundation for developing innovative anti-fibrotic treatment strategies <sup>2)</sup>.

Zhao et al. have provided a noteworthy contribution to the field of fibrosis and keloid research by leveraging cutting-edge single-cell technologies to dissect the cellular and molecular heterogeneity of keloid tissues. The identification of distinct fibroblast subpopulations with opposing roles in fibrosis is particularly promising for the development of targeted anti-fibrotic therapies. However, the study's limitations—chiefly the small sample size and the need for further functional validation—underscore the importance of cautious interpretation of these findings. Future research that addresses these issues and explores the interplay between multiple cell types in a broader patient cohort will be crucial for translating these insights into effective clinical interventions.

1)

LaRocca H, Macnab I. The laminectomy membrane. Studies in its evolution, characteristics, effects and prophylaxis in dogs. J Bone Joint Surg Br. 1974;56B:545–550.

Zhao S, Xie J, Zhang Q, Ni T, Lin J, Gao W, Zhao L, Yi M, Tu L, Zhang P, Wu D, Tang Q, Ma C, He Y, Li L, Wu G, Yan W. New Anti-Fibrotic Strategies for Keloids: Insights From Single-Cell Multi-Omics. Cell Prolif. 2025 Feb 4:e13818. doi: 10.1111/cpr.13818. Epub ahead of print. PMID: 39902627.

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