Background: Fibroblast heterogeneity and homeostasis has long been recognized in patients with systemic sclerosis (SSc). However, there is no common consensus on fibroblast subtypes, lineages, biological properties, signaling, and plasticity, which severely hampers our understanding of SSc pathogenesis.

Objectives: To comprehensively classify skin fibroblast populations from SSC patients.

Methods: We applied single-cell RNA sequencing on skin fibroblasts from two SSc patients and two health control (HC) with matched age and sex. Cell clustering was mainly determined by UMAP with batch effect correction. Differently expressed genes in each cell cluster were analyzed by Gene Set Enrichment Analysis (GSEA).

Results: With an unbiased approach, single-cell transcriptome analyses showed classified and defined eight fibroblast types in SSc skin and six in normal skin. The cell types seldom overlapped between the patients and HC. Extracellular interaction and collagen production were remarkably stronger in SSc fibroblasts. A subgroup of dramatic cell proliferation and activation was defined only in SSc fibroblast. Two subtypes responding inflammatory stimuli were only found in SSc patients. Furthermore, delineation of their differentiation trajectory was achieved by a machine learning method.

Conclusion: This collection of single-cell transcriptomes and the distinct classification of fibroblast subsets provide a new resource for understanding the fibroblast landscape and the roles of fibroblasts in SSc.

References: N/A

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TOFACITINIB INHIBITS TGF-β1-INDUCED ACTIVATED CELL FUNCTIONS OF MYOFIBROBLAST IN HUMAN LUNG FIBROBLAST POPULATIONS

F. Zhu1, X. Zhang1, Guangdong Provincial People’s Hospital, Guangdong Academy of Medical Sciences, Department of Rheumatology, Guangzhou, China

Background: Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a class of refractory diseases. Non-specific treatment with hormone and immunosuppressive agents is mostly used at present, but the effect is limited and the long-term survival rate is not improved [1]. A basic study showed that TOFA improved interstitial pulmonary disease, with significantly improved survival rate [2-4]. A subgroup of TOFA inhibit the function of HLFs migration and invasion, our study suggested that TOFA can significantly inhibit TGF-β1-induced HLFs migration.

Methods: Cell migration and invasion Assays

HLFs were incubated with TOFA for 72h, followed by TGF-β1 for 24h. DMEM serum-free medium was used to determine the cell density to 5.0 × 10^7/L, 600 uL medium containing 10% fetal bovine serum was added to the lower compartment of Transwell chamber, and 200 uL cell suspension was added to the upper compartment. Incubate in incubator for 12h. After fixation, staining and sealing, the cells were observed and counted under a microscope. At least 5 random fields, transmembrane cells were counted in each hole, and the mean value was taken.

Conclusion: TOFA can significantly inhibit TGF-β1-induced HLFs migration.

Figure 2. Effect of TOFA on HLFs invasion function (x200). Mean ± SEM. n = 5.

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