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The Impact of Lipids on Lung Fibrosis

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Abstract : Pulmonary fibrosis is a rare disease where uncontrolled wound healing processes damage the lung structure. Intensive changes within the extracellular matrix (ECM) and its interaction with fibroblasts have a major role in pulmonary fibrosis development. Among others, collagen is one of the main components of the ECM, and it is important for lung structure. In IPF, constant production of collagen by fibroblast, through TGFβ1-SMAD2/3 pathways, leads to an uncontrolled deposition of matrix and hence lung remodeling. Abnormal changes in lipid production, alterations in fatty acids (FAs) metabolism, enhanced oxidative stress, and lipid peroxidation in fibrotic lung and fibrotic fibroblasts have been reported; however, the interplay between the collagen and lipids is not yet established. One of the FAs influx regulators is Angiopoietin-like 4 (ANGPTL4), which inhibits lipoprotein lipase work, decreasing the availability of FAs. We hypothesized that altered lipid composition or availability could have the capability to influence the phenotype of different fibroblast populations in the lung and hence influence lung fibrosis. To prove our hypothesis, we aim to investigate lipids and their influence on human, animal, and in vitro levels. In the bleomycin model, treatment with the well-known metabolic drugs Rosiglitazone or Metformin significantly lower collagen production. Similar results were noticed in ANGPTL4 KO animals, where the KO of ANGPTL4 leads to an increase of FAs availability and lower collagen deposition after the bleomycin challenge. Currently, we study the treatment of different FAs on human lung para fibroblasts (hPF) isolated from donors. To understand the lipid composition, we are collecting human lung tissue from donors and pulmonary fibrosis patients for Liquid chromatography-mass spectrometry. In conclusion, our results suggest the lipid influence on collagen deposition during lung fibrosis, but further research needs to be conducted to understand the matter of this relationship.

Keywords : collagen, fibroblasts, lipidomics, lung, pulmonary fibrosis
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