genetically engineered PLD2$^{-/-}$ mice were intratracheally challenged with bleomycin (1.5 U/kg animal) for 14 days and markers of inflammation, EMT and fibrosis were determined. MLE-12 cells were treated with specific PLD1 or PLD2 inhibitors prior to bleomycin (10 mU/ml) challenge, and the role of PLD in EMT and apoptosis of alveolar epithelial cells was studied. Human lung fibroblasts were serum-starved (3h), pretreated with PLD1 or PLD2 inhibitors, and the effect of TGF-β (5 ng/ml) on differentiation of lung fibroblast to myofibroblast was determined. Intra-tracheal instillation of bleomycin in the mice for 14 days leads to the progression of fibrosis in the lung. The lung tissues of the bleomycin treated mice were found to have increased PLD2 protein expression, myofibroblast markers like α-SMA, fibronectin, mesenchymal markers like vimentin, inflammatory cytokines and collagen. Genetic deletion of PLD2 in mice attenuated bleomycin-induced lung inflammation and pulmonary fibrosis. *In vitro*, MLE-12 cells pretreated with either PLD1 or PLD2 inhibitor did not show a profound reduction either in apoptosis or the expression of transcription factors such as SNAIL, and other markers of EMT. However, MLE-12 cells pretreated with both PLD1 (250 nM) and PLD2 (500 nM) inhibitors were resistant to bleomycin-induced apoptosis, and exhibited reduced expression of SNAIL and mesenchymal markers. On the contrary, human lung fibroblasts pretreated with PLD1 and PLD2 inhibitors showed increased fibroblast to myofibroblast differentiation mediated by TGF-β. The present study suggests a role for PLD2 in bleomycin-induced PF. *In vitro*, inhibition of both PLD1 and PLD2 was necessary to attenuate bleomycin-induced EMT in epithelial cells and TGF-β mediated differentiation of fibroblasts to myofibroblasts. The *in vivo* and *in vitro* results identify the mechanism by which PLD regualtes PF and suggest PLD as a potential therapeutic target in pulmonary fibrosis. This work was supported by National Institutes of Health grant P01 HL98050 to VN.

## ID: 112 ROLE OF PHOSPHOLIPASE D IN IDIOPATHIC PULMONARY FIBROSIS

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Idiopathic pulmonary fibrosis (IPF) is a deadly interstitial disease that leads to scarring and fibrosis of the lung tissue. In pulmonary fibrosis, there is injury and denudation of the alveolar epithelium, which further leads to activation of fibroblasts which differentiate into myofibroblasts. This includes several mechanisms including epithelial to mesenchymal transition (EMT). In this study, we investigated the role of phospholipase D (PLD) in IPF and also its underlying mechanism like EMT and fibroblast proliferation and differentiation. An *in vivo* murine model of bleomycin-induced pulmonary fibrosis (PF) and *in vitro* models of murine alveolar type-II epithelial cells (MLE-12) and human lung fibroblasts were used. C57BL/6 and