WISP-1, a novel target for treatment of pulmonary fibrosis

Idiopathic pulmonary fibrosis (IPF) is characterised by formation of fibroblast foci and deposition of extracellular matrix (ECM) in the lung interstitium. This results in distorted lung architecture, impaired gas exchange and reduced respiratory function. Impaired crosstalk between alveolar type 11 (AT11) cells and subepithelial fibroblasts has previously been shown to contribute to ECM deposition in IPF.

This study investigated the gene regulatory networks behind AT11 cell dysfunction in IPF. Genetic analyses highlighted WNT-inducible signalling protein-1 (WISP-1) as a key mediator of AT11 cell dysfunction in IPF. WISP-1 was highly upregulated in AT11 cells in a mouse model of fibrosis and also in human lung tissue from patients with IPF.

The investigators treated murine primary AT11 cells with recombinant WISP-1 and induced epithelial-mesenchymal transition (EMT). EMT is recognised as a possible mechanism underlying the formation of fibroblast foci that occurs in IPF. Recombinant WISP-1 treatment of lung fibroblasts in vitro led to increased ECM deposition. Furthermore, WISP-1 neutralisation resulted in attenuation of lung fibrosis in mouse models as evidenced by decreased lung ECM deposition. A marked reduction in expression of genes associated with fibrosis and reversal of EMT gene expression was noted. Interestingly, this was shown to partially restore normal lung function and significantly improve survival.

Currently available treatment options for IPF are limited. This study puts forward WISP-1 as a novel potential therapeutic target in IPF. Whether or not the findings in mouse models will translate to humans remains to be seen.

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