European Respiratory Society
Annual Congress 2013

Abstract Number: 5429

Publication Number: P4896

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keyword 1: Idiopathic pulmonary fibrosis **Keyword 2:** Cell biology **Keyword 3:** Epithelial cell

Title: Wnt11 inhibits effects of transforming growth factor-beta1 (TGFβ1) on lung epithelial phenotype

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Body: TGFβ1 induces epithelial-mesenchymal transition (EMT) in alveolar type 2 cells in vitro & is implicated in idiopathic pulmonary fibrosis (IPF). Wnt11 is secreted by the lung mesenchyme. Literature suggests that Wnt signalling has crosstalk with the TGFβ1 signalling pathway & may play a role in IPF pathogenesis. There are currently no data on Wnt11 function in adult lungs; we investigated its putative role in EMT. A549 cells were treated with 10ng/ml TGFβ1 for 24 hours. We developed transgenic A549 cells which stably overexpress Wnt11. Mesenchymal marker expression (N-Cadherin, SLUG, Vimentin, α-Smooth Muscle Actin) were assessed using RT-qPCR. BrdU proliferation assays & wound healing assays were performed using these cells. Confocal microscopy was used to observe intracellular SMAD distribution. Following TGFβ1 treatment, A549-Wnt11 cells had reduced relative mRNA expression of mesenchymal markers compared with normal A549 cells. Using confocal microscopy SMAD was detected in nuclei of normal A549 cells, but not in nuclei of A549-Wnt11 cells, indicating inhibition of SMAD translocation to the nucleus. Wnt11 significantly inhibited A549 cell motility on wound healing assays (P=0.037) & significantly enhanced A549 cell proliferation on proliferation assays (P=0.0014).

Wnt11 appears to inhibit TGFβ1 mediated EMT in A549 cells, & inhibits epithelial wound repair which is abnormal in IPF.