European Respiratory Society
Annual Congress 2012

Abstract Number: 4717

Publication Number: P3760

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keyword 1: Idiopathic pulmonary fibrosis **Keyword 2:** Cell biology **Keyword 3:** Biomarkers

Title: Wnt11 inhibits epithelial-mesenchymal transition induced by TGFb1 in human type II alveolar epithelial cells

Dr. Domokos 29275 Bartis d.bartis@bham.ac.uk MD [1], Dr. Vijay 29276 D'Souza v.k.dsouza@bham.ac.uk [1], Dr. Judit E. 29277 Pongracz judit.e.pongracz@aok.pte.hu [2] and Dr. David R. 29278 Thickett d.thickett@aok.pte.hu [1]. [1] Respiratory Research Laboratories, University of Birmingham, United Kingdom, B15 2WB and [2] Department of Medical Biotechnology, University of Pecs, Hungary, H-7643 .

Body: Increased activity of TGFβ1 plays a crucial role in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Alveolar type II cells (ATII) undergo EMT expressing mesenchymal markers when exposed to a high concentration of TGFβ1 in both in vitro and in vivo models. Mesenchymal signals might contribute to the differentiation and regeneration of pulmonary epithelium. Wnt11 is a secreted glycoprotein known to be expressed in the mesenchyme of the embryonic lung. We constructed a 3-dimensional (3D) human tissue model of primary human pulmonary cells to mimic epithelial-mesenchymal interactions in the lung. Our results indicate that human lung fibroblasts are a source of Wnt11 in the lung tissue model. ATII cells isolated from human lung samples were treated with recombinant TGFβ1 and/or Wnt11. Expression levels of the EMT markers N-cadherin, Vimentin, alpha smooth musle actin (αSMA) and SLUG were determined by qPCR and immunofluorescence. We found that Wnt11 inhibits EMT induced by TGFβ1 in ATII monolayers and in 2D and 3D ATII+fibroblast co-cultures. Wnt11 treatment resulted in decreased expression of EMT markers compared to TGFβ1 treated cell cultures.

We propose that the pulmonary mesenchyme might contribute to the homeostasis of epithelial cells by secreting Wnt11. The finding that effects of TGFβ1 can be antagonized by Wnt11 may mark it as a potential therapeutic target in the fibrotic diseases of lung.