European Respiratory Society
Annual Congress 2013

Abstract Number: 7186

Publication Number: P4880

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keyword 1: Lung growth/development **Keyword 2:** Neonates **Keyword 3:** Airway smooth muscle

Title: FGF10 identifies early lipofibroblast progenitors and controls their fate during embryonic lung development

Dr. Denise 1304 Al Alam dalalam@chla.usc.edu [1], Dr. Elie 1305 El Agha elieagha@gmail.com [2], Dr. Soula 1306 Danopoulos sdanopoulos@chla.usc.edu [1], Dr. Virender 1307 Rehan vrehan@labiomed.org MD [3] and Dr. Saverio 1308 Bellusci sbellusci@chla.usc.edu [1,2]. [1] Surgery, Children's Hospital Los Angeles, Los Angeles, CA, United States, 90027 ; [2] Department of internal medicine, ECCSP, Giessen, Germany and [3] Department of Neonatology, Harbor UCLA Medical Center, Los Angeles, CA, United States .

Body: Introduction: Lipofibroblasts (LIFs) are lipid-containing fibroblasts found in the late fetal and postnatal lung parenchyma. LIFs assimilate lipids and transfer triglycerides to adjacent alveolar epithelial type II cells to elaborate surfactant. Aims: Although LIFs have been studied in postnatal lungs, their cellular origin and mechanism of differentiation are unknown. We aim to determine the origin of LIFs and the molecular pathway that control their fate. Methods: Using Fgf10-LacZ and Fgf10iCre mouse lines, we analyzed the expression of LIFs markers in the Fgf10-positive cells in situ and after sorting. In addition, we used in vivo knockdown of FGFR2b ligand activity from E14.5 to E18.5 and Fgf10 hypomorphs as well as in vitro models (WI-38, NIH3T3-L1 cell lines and primary cultures of fibroblasts) to test whether FGF10 is capable on acting directly on the mesenchyme to promote LIFs differentiation. Results: We demonstrated that LIFs express Fgf10 and that Fgf10-positive cells permanently labeled at embryonic days E11.5 or E15.5 give rise to LIFs. In addition, in vivo knockdown of FGFR2b ligand activity as well as reduction of Fgf10 expression led to decreased expression of LIF markers at E18.5. Using primary culture of lung mesenchyme as well as WI-38 human LIF progenitor cells and NIH3T3-L1 adipocyte progenitor cells, we demonstrate that recombinant FGF10 is capable of directly acting on the mesenchyme to trigger the commitment of these cells to the adipogenic lineage. Moreover, FGF10 also antagonizes TGFβ1-induced myofibroblast transdifferentiation of Fgf10-positive cells. Conclusion: Our results demonstrate the essential role of FGF10 signaling in LIF formation.