European Respiratory Society
Annual Congress 2012

Abstract Number: 6024

Publication Number: 3103

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keywords: no keyword selected

Title: LSC 2012 abstract – TGF-β1 regulates the epithelial supportive capacity of mesenchymal stromal cells

Jonathan 600128 McQualter jlmcq@unimelb.edu.au [1], Rosa 600129 McCarty [1] and Ivan 600130 Bertoncello [1]. [1] Department of Pharmacology, University of Melbourne, Melbourne, United Kingdom .

Body: Despite recent advances in biomarker profiling, prospective isolation and clonogenic assay of putative lung stem cells their regenerative capacity remains ill-defined. On that account we have developed a clonogenic colony-forming assay that has enabled us to identify a population of multi-potent lung epithelial stem cells (EpCAMhi CD49fpos CD104pos CD24low) that are able to self-renew and give rise to airway and alveolar epithelial cell lineages. However,the intrinsic regenerative potential of stem cells is conditional upon their interaction with permissive and restrictive microenvironmental cues. On this note, we have shown that the proliferation and differentiation of lung epithelial stem cells in vitro is dependent on co-culture with endogenous lung mesenchymal stromal cells (EpCAMneg Sca-1pos), or mesenchyme-derived growth factors including FGF-10 and HGF. On the flip side, we have shown that more differentiated mesenchymal stromal cells (FGF-10low α- SMApos) are unable to support epithelial colony formation. Importantly, we have shown that the capacity of mesenchymal stromal cells to support epithelial stem cells is regulated by TGF- β1 and can be reversed by blockade of SMAD2/3 phosphorylation downstream of TGF-β activation. This data suggests that TGF-β mediated mesenchymal differentriation in chronic lung diseases may obstruct epithelial regeneration.