European Respiratory Society
Annual Congress 2013

Abstract Number: 6010

Publication Number: P4883

Abstract Group: 3.3. Mechanisms of Lung Injury and Repair

Keywords: no keyword selected

Title: LSC 2013 abstract - Unravelling VEGF165 signalling in the lung

Ms. Khadija Ourradi Khadija.Ourradi@bristol.ac.uk [1], Thomas Blythe [1], Shaney Barratt [1], Caroline Jarett [1], Gavin Welsh [1] and Ann Millar [1]. [1] School of Clinical Sciences, University of Bristol, Bristol, United Kingdom .

Body: Vascular endothelial growth factor (VEGF) is a potent mitogenic, angiogenic and permeability factor implicated in both the development of lung injury and repair in several respiratory diseases such as ARDS and IPF. $VEGF_{165}$ acts through VEGF receptors in particular VEGFR-2, leading to a complex network of signalling pathways resulting in changes to cell permeability, migration and proliferation; unexplored in the lung. We have investigated the downstream signalling mechanisms regulated by $VEGF_{165}$ in pulmonary and systemic endothelial cells. HUVEC and Human Lung Microvascular Endothelial Cells (HMVEC-L) were treated with $VEGF_{165}$. Phosphorylations of VEGFR-2 ($tyr^{1175}$and tyr^{1214}) were measured along with phosphorylation/activation of pMEK1/2, p44/42MAPK (regulating cell proliferation) and eNOS protein (involved in cell permeability). The downstream effects of $VEGF_{165}$ on cell permeability was assessed by Endohm, Electrical Cell-Substrate Impedance Sensor (ECIS) and FITC-BSA passage and changes in VE-cadherin cell distribution was determined by immunofluorescence. Phosphorylation of VEGFR-2 at tyr^{1175} and tyr^{1214} was induced between 2 and 10min (5 fold increase). Activation of pMEK1/2 and p44/42MAPK showed a similar time course to that of VEGFR-2 (>5 fold). Phosphorylation of eNOS was also observed (>2 fold) and indeed $VEGF_{165}$ increased cell permeability in both cell types (Huvec $p<0.001$) (Hmvec-l $p<0.01$) with the different measurement. In both cell types, significant changes in VE-cadherin cellular distribution were generated by VEGF. $VEGF_{165}$ induces responses in HUVEC and HMVEC-L cell behaviour suggesting different pathways for the regulation of mitogenesis or permeability identifying potential therapeutic targets.