European Respiratory Society
Annual Congress 2013

Abstract Number: 7212

Publication Number: P5154

Abstract Group: 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

Keyword 1: Cell biology **Keyword 2:** Biomarkers **Keyword 3:** Pulmonary hypertension

Title: A novel and translatable cell assay for the study of vascular signalling in pulmonary hypertension

Mr. Daniel M. 1543 Reed daniel.reed09@imperial.ac.uk [1], Dr. Peter M. 1544 George p.george@imperial.ac.uk MD [1], Dr. Catherine 1545 Francis catherinefletcher@nhs.net MD [1], Ms. Laura B. 1546 Feyereisen laura.feyereisen10@imperial.ac.uk [1], Dr. William 1547 Swain william.swain@actelion.com [2], Dr. Marc 1548 Iglarz marc.iglarz@actelion.com [2], Dr. Amanda 1549 Wan amanda.wan@actelion.com [2], Dr. Benjamin 1550 Garfield benjamin.garefield@nhs.net MD [1], Dr. John 1551 Wort s.wort@imperial.ac.uk MD [1] and Prof. Jane A. 1552 Mitchell j.a.mitchell@imperial.ac.uk [1]. [1] Dept. of Cardiothoracic Pharmacology, NHLI, Imperial College London, London, United Kingdom, SW3 6LY and [2] Actelion Pharmaceuticals UK, Actelion, London, United Kingdom, W4 4AL .

Body: Pulmonary hypertension (PH) is a rare but severe disease. Endothelial and vascular smooth muscle cells are critically involved in the pathology of PH. However, pulmonary vessels are not accessible in most patients. Blood outgrowth (BO) vascular cells are derived from progenitors and are potentially valuable, highly translatable models. Here, we show for the first time that endothelial cells (BOEC) and putative smooth muscle cells can be grown out from the blood of patients with PH. BOEC from patients (n=2) aligned under complex shear conditions in a way characteristic of endothelial cells, expressed VE-cadherin and released endothelin-1. Autologous vascular smooth muscle cells were isolated from the same patients' peripheral blood samples and displayed a typical 'hill and valley' morphology (Fig A). As interferon (IFN) signalling is thought to be relevant to vascular dysfunction, responses of BOEC from PH patients (n=3) to IFNα and IFNγ (30ng/ml) were compared to healthy donor cells (n=4-6). IP10 (CXCL10) was measured as a ubiquitous readout of IFN signalling. BOEC from PH patients released more IP10 in response to IFNs (Fig B). The ability to derive both endothelial and smooth muscle cells from individual patients with PH represents a key step forward in translational and personalised research in this condition.

This study was supported by an unconditional educational award from Actelion.