Conditioned media from human pulmonary arterial endothelial cells treated with hepcidin or haemoglobin cause proliferation and migration of human pulmonary artery smooth muscle cells

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Introduction: Pulmonary arterial hypertension (PAH) is characterised by vascular remodelling of pulmonary arterioles. Disrupted iron homeostasis including subclinical haemolysis are implicated in PAH, although exact mechanisms remain unknown. Interactions linked to altered iron handling consequent to release of mediators by human pulmonary artery endothelial cells (hPAECS) and/or human pulmonary artery smooth muscle cells (hPASMCs) may be important in this regard.

Objectives: This study explored proliferative and migratory responses in hPASMCs linked to the primary exposure of hPAECs to indices of dysregulated iron homeostasis i.e. hepcidin or haemoglobin.

Methods: hPAECs were challenged with haemoglobin (10uM) or hepcidin (100-1000ng/mL). Proliferation and migration of hPASMCs were analysed using xCELLigence RTCA instrument by measuring the changes in cell index / impedance.

Results: Novel findings demonstrate that media conditioned with hepcidin for 48 h from hPAECs increased proliferation of hPASMCs by 24% (95% CI 0.256- 47.9, $P<0.05$) after 48 h of treatment. Additionally, 24 h conditioned media from both hepcidin and haemoglobin treated hPAECs caused 3.27 and 2.28 fold increases in migration respectively in hPASMCs.

Conclusion: These findings highlight a direct role for variant iron homeostasis in hPAECs which is linked to subsequent functional responses in hPASMCs of importance to vascular remodelling. These studies may provide novel insights regarding mechanisms for haemoglobin and hepcidin driven proliferative and migratory responses of relevance to PAH.