Ferroportin is expressed in human pulmonary artery smooth muscle cells: implications for pulmonary arterial hypertension

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Background Pulmonary Arterial Hypertension (PAH) is a rare but fatal condition manifested by pulmonary vascular remodelling, increased pulmonary vascular resistance and right-heart failure. Disturbance in iron handling and anaemia, caused by elevated iron-regulatory hormone hepcidin, is observed in PAH. Ferroportin, the only known cellular iron-export protein, is downstreamed by hepcidin. As such, iron supplementation as a therapy is currently under clinical trial. However, it is also known that iron is both pro-oxidant and pro-proliferative. Latest evidence also points to sub-clinical haemolysis and the presence of free haemoglobin in PAH patients. We hypothesised that ferroportin would be expressed; be responsive to hepcidin challenge and have implications for the proliferation of human pulmonary artery smooth muscle cells (hPASMCs).

Methods The mRNA levels of ferroportin were measured by RT-PCR. The protein expression was detected by western-blot analysis and quantified by ELISA. The sub-cellular distribution of ferroportin was quantified by ELISA. The sub-cellular distribution of ferroportin would be expressed; be responsive to hepcidin challenge and have implications for the proliferation of human pulmonary artery smooth muscle cells (hPASMCs).

Results Basal ferroportin mRNA was detected in hPASMCs, but basal ferroportin was uniformly distributed in the cells; however hepcidin challenge caused decrease in ferroportin protein levels. Basal ferroportin was uniformly distributed in the cells; however hepcidin challenge led to intense punctate-vesicular staining. Finally, exposure to free haemoglobin alone or along with hepcidin increased proliferation of hPASMCs by 13.6% and 12.4% respectively. Interestingly, pre-incubation of the cells with LY2928057 partly reversed this effect.

Conclusion This is the first report of ferroportin expression and regulation in hPASMCs. We suggest that targeting and manipulating the hepcidin-ferroportin axis using LY2928057 might prove a novel therapeutic approach for PAH.

Vascular endothelial cell growth factor-A (VEGF-A) signalling and neovascularisation of pulmonary endarterectomy material in chronic thromboembolic pulmonary hypertension (CTEPH)

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Background Despite recent advances in the medical treatment of patients with CTEPH, relatively little is understood surrounding the underlying pathological mechanisms. Many patients have a historical documented venous thromboembolic event (VTE) and consequently, failed resolution of an acute VTE has been proposed as a key initiating factor in the subsequent development of CTEPH. Here we investigated VEGF-A levels, a key regulator of angiogenesis, in CTEPH patients prior to and following...