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EXOSOME CHARACTERIZATION TO IDENTIFY PROTEINS UNIQUE TO PAH

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Introduction/Aim: Pulmonary arterial hypertension (PAH) is a fatal disease caused by intrinsic remodelling of the pulmonary small blood vessels that leads to increased arterial pressure and ultimately right side heart failure. There is incomplete knowledge surrounding the pathogenesis of the disease and a lack of treatment options. Exosomes are cellular vesicles that mediate cell-to-cell communication and could act as biomarkers of disease and have potential therapeutic benefits as they also contribute to pathogenesis. We hypothesised that the protein expression profile of exosomes from PAH patient blood outgrowth endothelial cells (OECs) would be different to that of controls.

Methods: OECs were isolated and cultured from 15mL of PAH (n = 4) or control (n = 4) peripheral blood. Exosomes were isolated from OEC cultured media via differential centrifugation, and characterised with a NanoSight, TEM and SEM. Mass spectrometry was used to generate exosome protein profiles.

Results: Exosomes were positively identified as 40-200nm via NanoSight, TEM and SEM. There were 500 proteins common to all controls, with 105 proteins that were distinct from PAH patients, and 85 proteins that were significantly upregulated in the PAH patients in comparison to the controls, including SPARC ($P < 0.005$), a protein responsible for pathological responses of tissue after injury through regulation of cell growth. There were 440 common proteins across all PAH patients and out of these 45 were distinct from the controls, with 16 proteins significantly downregulated in the PAH patients in comparison to controls (Figure 1).

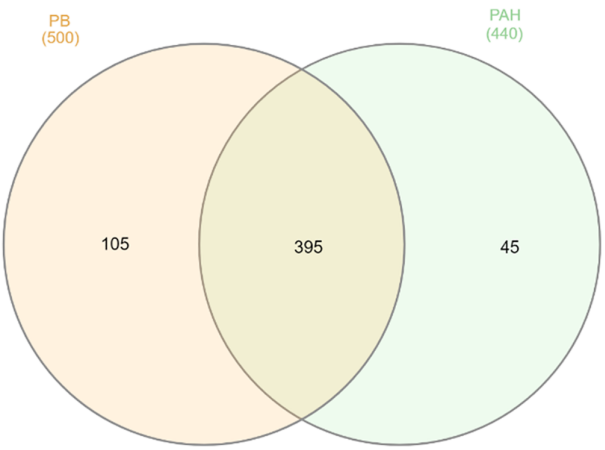

Figure 1. Cross over of exosome proteins derived from OECs identified by mass spectrometry in healthy controls (PB) and PAH patients, highlighting 105 proteins unique to healthy controls and 45 proteins unique to PAH patients

Conclusion: This work has enabled the identification of new proteins that could have potential as therapeutic targets, such as SPARC. Further investigation into these newly identified proteins will contribute to understanding of disease pathogenesis and further treatment options using cell therapies.

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