Introduction Pulmonary hypertension (PH) is characterised by elevated pulmonary arterial pressures, inappropriate apoptosis and vascular remodelling. Animal models fail to replicate such cellular changes. Current therapies target several mediators including endothelin-1 (ET-1). Mortality rates remain high, suggesting other influential biochemical pathways have been overlooked. Intermedin is a potent pulmonary vasodilator acting on receptor complexes comprising calcitonin receptor-like receptor (CRLR) and one of three receptor-activity modifying proteins (RAMPs).

Aims (i) Characterise Intermedin, Adrenomedullin and receptor component distribution across human pulmonary cell-types; (ii) examine effects of simulated hypertension±IMD on pulmonary smooth muscle cell (PSM).

Methods The Flexcell apparatus was used to simulate hypertension. Cell viability was measured by trypan blue assay. Gene expression was quantified by qRT-PCR. Protein levels were assessed by indirect-immunofluorescence techniques and immunoblotting.

Results IMD and AM were most abundant in pulmonary microvascular endothelial cells (PMVEC) and PSM respectively. CRLR was expressed less abundantly than RAMPs1-3; RAMP2 predominated in all cell types. PreproET-1 and preproIMD mRNAs increased maximally 19 fold ($p<0.0001$, 48 h) and 2-fold ($p<0.01$, 72 h) respectively in PSM after simulated hypertension. IMD 20 ρmol l-1 improved cell viability in flexed cells and CRLR/RAMP mRNA up-regulation was also observed ($p<0.01$ vs control), maximally at 48 h.

Discussion IMD and its receptor components were each distributed differentially across human pulmonary cell-types. PH was evidenced in flexed cells by up-regulated ET-1 expression and reduced cell viability. Delayed up-regulation of IMD expression supports a counter-regulatory cytoprotective function for this peptide in human PH.

P13 **THE ROLE OF THE PEPTIDE INTERMEDIN IN A NOVEL MODEL OF PULMONARY HYPERTENSION**

doi:10.1136/heartjnl-2012-303148a.18

D Holmes,* D Bell, M Harbinson, M Campbell. *School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, UK*