vs. H9c2 EVs 100 nm size, 2.5 × 10^8 particles/ml). EVs isolated from 1 μM AngII treated H9c2 cardiomyocytes significantly increased cell area of recipient H9c2 cardiomyocytes (control EV treated 3291.1±90.1 μm^2 vs AngII EV treated 5252.3±125.4 μm^2, p<0.001). EVs isolated from 1 μM Ang-(1-7) treated H9c2 cardiomyocytes significantly reduced AngII peptide induced increase in cell area in a dose dependent manner in recipient H9c2 cardiomyocytes (100 nM AngII +Control EVs 5566.3±139.0 μm^2 vs 100 nM AngII+Ang-(1-7) EVs 4212.7±132.1 μm^2, p<0.001).

Summary/conclusions Collectively these data suggest that there are distinct sub-populations of EVs released that differ between NRCF cells and H9c2 cardiomyocytes. We have shown that H9c2-derived EVs can elicit deleterious or cardioprotective effects on recipient H9c2 cardiomyocytes depending on the condition of the parental cells.

6 RESISTIN MEDIATES SEX-DEPENDENT EFFECTS OF PERIVASCULAR ADIPOSE TISSUE ON VASCULAR FUNCTION IN THE SHRSP

[1]Sarah McNeilly*, [1]Heather Y Small, [1,2]Sheon Mary, [1]Adam Sheikh, [1]Christian Delles. *[1]BHF Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Scotland, UK; [2]Department of Biochemical Sciences, CSIR-National Chemical Laboratory, India*

10.1136/heartjnl-2017-311433.6

Introduction Premenopausal women are relatively protected against hypertension compared to males. Oestrogen levels have been identified as a potential underlying cause, but many of the pathophysiological mechanisms remain to be determined. Altered perivascular adipose tissue (PVAT) function has been identified to have vasoactive effects. However, in hypertension, sex-dependent differences of PVAT have not yet been explored.

Hypothesis Sex-dependent effects of PVAT mediate altered vascular function in hypertension.

Approach and result The effect of PVAT was investigated on resistance vessels of 16 week old male and female stroke-prone spontaneously hypertensive rats (SHRSP). This preclinical model of hypertension presents with a sex-difference in the development of hypertension comparable to humans. Wire-myography was used on 3rd order mesenteric vessels to assess vascular function. Noradrenaline mediated vasoconstriction was increased in SHRSP males compared to females (maximum contraction: male +PVAT 113.3±1.1% vs female +PVAT 91.4%±11.36%). K_{ATP} channel-mediated vasorelaxation by cromakalim was impaired in males compared to females (maximum relaxation: male +PVAT 46.9±3.9% vs female +PVAT 97.3%±2.7%). A cross-over study assessing function of male PVAT on female vessels and vice versa confirmed the reduced K_{ATP} mediated vasorelaxation induced by male PVAT (maximum relaxation: female +$PVAT_{female}$ 90.6 ±1.4% vs female +$PVAT_{male}$ 65.8%±3.5%). To explore the cause of sex-dependent differences in PVAT an adipokine array with subsequent western blot validation was carried out. This identified resistin as a potential modifier of vascular reactivity. Resistin was increased by approximately 2-fold in SHRSP male mesenteric PVAT. Further wire-myography experiments with male and female vessels pre-treated with resistin (40 ng/ml) showed no difference in response to noradrenaline. However, vasorelaxation in response to cromakalim was significantly impaired in resistin treated female vessels, similar to levels observed in male vessels (maximum relaxation: female +PVAT 97.3±0.9% vs female +PVAT +resistin[40 ng/ml] 36.8% ±2.3%).

Conclusion These findings indicate a novel role for resistin in sex-dependent PVAT mediated vascular function in hypertension through a K_{ATP} channel mediated mechanism.

7 QUANTIFYING THE BIO-DISTRIBUTION OF TRANSPLANTED HESC-ECS IN A MURINE MODEL OF HLI BY QPCR

[1]Lucija Fleisinger*, [1]Mark G MacAskill, [2]Joanne C Mountford, [1]Andrew H Baker, [1]David E Newby, [1]Patrick WF Hadoke. *[1]University/BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK; [2]Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK*

10.1136/heartjnl-2017-311433.7

Introduction Beneficial effects of stem/progenitor cell therapies for the treatment of ischaemic diseases have been established; however, there remains conflicting evidence on whether cells act by incorporation into the existing vasculature or by paracrine effects.

Objective This study aims to quantify the bio-distribution of transplanted, proangiogenic, human embryonic stem cell-derived endothelial cells (hESC-ECs) in a murine model of hind limb ischaemia over 21 days using qPCR-detection of human DNA.

Methods CD1 nude mice (male, 6–8 weeks old; n=6 per group) underwent femoral artery ligation followed by injection with hESC-ECs into ischaemic muscle of the hindlimb. Mice were sacrificed at 0 hour, 4 hour, 24 hour, 7d, 14d, and 21d post-transplantation, and DNA extracted from the hind limb. A paired-qPCR assay was run with a set of human-specific and mouse-specific primers to allow for detection of hESC-ECs in mouse tissue.

Results A standard curve was constructed using mixtures of DNA extracted from mouse tissue and a population of hESC-ECs. The mean percentage of human cells at each time-point was determined accordingly. At the first time-point (0 hour), 1.77%±0.55% human cells were present within the ischaemic limb, with no significant change at 4 hour post-injection. However, by 24 hour and 7 days post-injection, the% human cells present significantly decreased to 0.67%±0.24% (p=0.05) and 0.35%±0.09% (p=0.05) respectively. At 14 and 21 days post-injection, the level of human DNA present had decreased to background levels.

Conclusion Our results suggest the majority of injected hESC-EC cleared from the injection site within the first 24 hours, with the remainder of the cells no longer present at 14 days post-injection. This is consistent with imaging data obtained prior to this study, and suggests that injected hESC-ECs improve perfusion in the mouse ischaemic limb by a paracrine mechanism rather than direct incorporation into the existing vasculature.

Poster Presentations

8 GENERATING A GENOMIC-WIDE TRANSCRIPTOMIC ATLAS OF THE MAMMALIAN CARDIOVASCULAR SYSTEM

[1]Hiu-Gwen Tsang*, [1]Emily L Clark, [1]Stephen J Bush, [1]David A Hume, [2]Brendan M Corcoran, [1]Vicky E MacRae, [1]Kim M Summers. *[1]The Roslin Institute, The University of Edinburgh, Easter Bush, UK; [2]The University of Edinburgh, Hospital for Small Animals, Easter Bush, UK*

10.1136/heartjnl-2017-311433.8

The various highly specialised tissues and structures that form the cardiovascular system enable the transport of blood, oxygen and other important molecules throughout the body. Perturbations in this system increase the risk of developing cardiovascular-related disease.

A sheep cardiovascular transcriptomic atlas was generated using RNA-seq to explore gene expression patterns in the mammalian cardiovascular system. Tissues included the cardiac valves, as well as left and right auricles and ventricles. Detailed functional clustering of the sheep transcriptome was performed, where transcripts were grouped according to their expression pattern. This analysis, using the innovative Miru (Kajeka) bioinformatics tool, was based on a gene-to-gene comparison of the expression patterns across analysed samples, using a Pearson correlation matrix (correlation value $R \geq 0.99$). Expressed genes in clusters were grouped together according to region-specific roles and specialised cellular functions. Notably, one cluster contained genes with high expression in the auricles in this dataset. The cluster genes were involved in cation channel activity (GO term enrichment analysis returned a Benjamini corrected p-value of $3.4 \times 10–2$). Genes in this cluster included potassium channel subfamily K member 3 (KCNK3; also known as TWIK-related acid-sensitive K+ channel, TASK1), potassium voltage-gated channel subfamily J member 3 (KCNJ3), and myosin light chain 4 (MYL4). Additionally, a number of genes within this cluster have been implicated in atrial fibrillation, and further genes in this cluster may also be important in atrial function.

This dataset provides a highly valuable resource for understanding gene expression in the mammalian cardiovascular system.

9 $COCL_2$ INDUCED CARDIOTOXICITY ASSOCIATED WITH COCR ALLOY ORTHOPAEDIC IMPLANTS- AN *IN VIVO* AND AN *IN VITRO* STUDY

[1]Sarunya Laovitthayanggoon*, [1]M Helen Grant, [1]Catherine J Henderson, [2]Rothwelle J Tate, [2]Susan Currie. *[1]Department of Biomedical Engineering, University of Strathclyde, Glasgow, UK; [2]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK*

10.1136/heartjnl-2017-311433.9

Cobalt/chromium (Co/Cr) alloy metal-on-metal bearings used in prosthetic hip replacements can cause adverse effects in some patients because they release metal ions into the bloodstream during wear. Co toxicity may be a cause of many severe systemic manifestations including neurologic and cardiac symptomatology.

This study examines the effects of chronic Co exposure in rats treated for 28 days with $CoCl_2$ (single i.p. injection of 1 mg/kg, daily) and examines Co uptake *in vitro* into primary adult cardiac fibroblasts (CFs). Co treatment was associated with accumulation into various organs with significant increases detected in liver, kidney and heart (245.31 ± 23.64, 204.80 ± 11.19 and 41.04 ± 4.77 µg/L respectively). Echocardiography performed on the same animals showed functional changes correlating with compromised cardiac contractility. Fractional shortening was significantly reduced in $CoCl_2$-treated rats following 28 days treatment when compared with control animals ($54.01\% \pm 0.90\%\%$ vs $60.29 \pm 0.53\%\%$, $n=6$, $p \leq 0.01$) and there was evidence of diastolic dysfunction. In order to investigate how Co may accumulate in the heart, primary adult CFs were isolated and uptake of $CoCl_2$ into CFs was compared with uptake into a standard fibroblast 3T3 cell line (3T3s). Uptake of metal ions was measured using inductively coupled plasma mass spectrometry. Co uptake into both 3T3s and CFs increased to between 0–50 and 0–120 µg/L, respectively as the medium concentration of Co (0–300 µM) increased. Interestingly, uptake of Co into CFs was significantly greater than into 3T3 cells. The greater accumulation of $CoCl_2$ into CFs suggests that Co ions *in vivo* could accumulate in these cells and have functional consequences on cardiac performance. Overall, our data provides strong evidence that Co accumulates in the heart resulting in cardiac dysfunction. Importantly, we have shown for the first time that Co could accumulate in the heart via efficient uptake into CFs. Future work will focus on determining the underlying mechanism for uptake which could have important therapeutic implications.

10 MACROPHAGE-DERIVED WNTS ARE REQUIRED FOR SCAR-FREE REGENERATION OF THE NEONATAL MOUSE MYOCARDIUM

[1]Castellan RFP*, [2]Thompson M, [3]Soong DYH, [1]Mylonas KJ, [1]Thomson A, [1]Moran CM, [2]Kitsis RN, [3]Pollard JW, [1]Gray GA. *[1]Centre for Cardiovascular Science, QMRI, The University of Edinburgh, Edinburgh, UK; [2]Albert Einstein College of Medicine, Bronx, UK; [3]MRC Centre for Reproductive Health, QMRI, The University of Edinburgh, Edinburgh, UK*

10.1136/heartjnl-2017-311433.10

Objective In contrast to the adult, neonatal mice regenerate their myocardium following injury, at least during the first week after birth.[1] Macrophages (Mϕ) contribute to vessel formation and scar removal following neonatal myocardial infarction (MI)[2]. In the kidney[3] liver[4,7] and gut[5] Mϕ-derived WNTs are required for scar free regeneration following injury. Secretion of WNTs is dependent on acylation by Porcupine (PORCN). In the present study it was hypothesised that neonatal cardiac regeneration would be impaired in mice with Csf1r-Cre driven Mϕ specific *Porcn* deletion.[5]

Methods Csf1r-EGFP(MacGreen), $Porcn^{fl}/Csf1r^{Cre-ve}$ and $Porcn^{fl}/Csf1r^{Cre+ve}$ mice underwent coronary artery ligation at post-natal day 1 (P1). Functional loss 1 day after MI, and recovery by P21 were assessed by high-resolution ultrasound. Heart sections were stained with isolectin B4 (vessel density) and picrosirius res (fibrosis). Myocardial gene expression was determined by PCR array in wild-type (WT) mice after injury.