Poster Presentations

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

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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

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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

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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.