206 THE TRANSPLANTATION OF SCA-1+/PW1+/PAX7- SKELETAL MUSCLE-DERIVED INTERSTITIAL PROGENITOR CELLS (PICS) IMPROVES CARDIAC FUNCTION IN MICE SUBJECTED TO MYOCARDIAL INFARCTION

Prashant Jay Ruchaya*, Sachin Amin, Giulia Gritti, Georgina Ellison-Hughes. *King's College London*

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Introduction Stem cell-based regenerative therapies are fast becoming an attractive and highly promising treatment for heart disease and failure. Sca-1^+/$PW1^+$/$Pax7^-$skeletal muscle-derived interstitial progenitor cells (PICs) regenerate adult skeletal and smooth muscle. Recently, we showed that PICs can differentiate into cardiomyocyte-like cells *in vitro*. These findings have subsequently opened the potential for PICs to be used as a regenerative therapy in heart failure..

Aim We sought to investigate the *in-vivo* physiological effects of transplantation of PICs in mice subjected to myocardial infarction (MI).

Methods Myocardial infarction was induced through the ligation of the left anterior descending coronary artery in 8–9 week old male C57BL/6 mice. 500,000 Sca-1^+/$PW1^+$/$Pax7^-$ PICs (MI+PICs) or PBS (MI-PBS) were transplanted intramyocardially in two regions of the border zone, immediately after MI induction. SHAM mice underwent the same surgical procedure, without ligating the coronary artery, or the intramyocardial transplantation of PICs or PBS. Echocardiography was performed prior to surgery (baseline), and week 3 post-MI and cell transplantation. Mice were sacrificed at 3 weeks post-MI, and histology and Masson Trichrome staining was performed to assess infarct size and level of fibrosis.

Results A significant ($p<0.05$) improvement in Ejection Fraction (EF) was observed in MI mice transplanted with PICs (MI-PICs), compared to MI+PBS at week 3 post-MI (55.8 ±4.2% vs. 35.2±3.6%, respectively). However, this improvement of EF in MI+PICs remained significantly ($p<0.05$) lower, compared to SHAM (71.1±0.9%) at matched time points, and to corresponding baseline (69.6±0.7%) levels. A similar trend in Fractional Shortening (FS) was observed, where the MI+PICs group showed a significant ($p<0.05$) improvement, compared to the MI+PBS group (29.2 ±2.6% vs.17.0±2.0%, respectively). The improvement in FS remained significantly ($p<0.05$) lower in the MI+PICs group, compared to SHAM (38.8±1.4%) and to corresponding baseline levels (38.8±0.5%). Infarct size and fibrosis significantly ($p<0.05$) decreased in the MI-PICs group (24.2±2.2% of LV), compared to the MI-PBS group (40.2±2.6% of LV).

Conclusions Transplantation of skeletal muscle-derived Sca-1^+/$PW1^+$/$Pax7^-$ PICs into the myocardial infarcted myocardium improves cardiac function, and reduces infarct size. Although the mechanism of action needs to be clarified, PICs could be a promising stem/progenitor cell type for the treatment of heart failure.

207 VASCULAR SMOOTH MUSCLE CELL HETEROGENEITY AND PLASTICITY

[1]Annabel Taylor*, [2]Lina Dobnikar, [2]Mikhail Spivakov, [1]Helle JÃƒÂ¸rgensen. *[1]Division of Cardiovascular Medicine, University of Cambridge*; *[2]Nuclear Dynamics ISP, Babraham Institute*

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Introduction Vascular smooth muscle cells (VSMCs) show inherent plasticity, enabling their phenotypic switch into a synthetic state for vascular repair and remodelling. Under inflammatory conditions, this contributes to atherosclerotic plaque development, with VSMCs demonstrated to produce multiple plaque-resident cell types. However, only a small fraction of VSMCs participate in disease associated proliferation[1] and it is unclear if this is a defined subset within the heterogeneous population.

Methods Here we performed transcriptional profiling of dissociated VSMCs from two discrete aortic regions; the plaque-susceptible aortic arch (AA) and resistant descending thoracic aorta (DT). Differentially expressed genes were identified using both conventional and single cell RNA sequencing. This differential expression was then validated by RT-qPCR and single molecule RNA fluorescence *in situ* hybridisation (smRNA-FISH), implemented to interrogate candidate gene expression at a single-cell level.

Results RNA sequencing analysis demonstrated differential expression of 227 genes between the AA and DT regions, with consistency in the profiling data from conventional and single cell sequencing. These results correlate with earlier work to profile these regions; for example, we found upregulation of homeobox genes in the DT relative to the AA, which has been previously observed[2]. However, many of the genes identified are distinct from those previously characterised and our single cell analysis demonstrated heterogeneity between individual cells within the same region. In particular, certain genes were highly expressed in only a subset of AA cells, including Pde1c, an enzyme shown to promote VSMC proliferation[3]. Patterns in expression were validated for candidate genes, selected by VSMC or disease relevance. This showed similar fold changes in expression between the two regions by RT-qPCR and RNA sequencing, with ongoing smRNA-FISH investigations into their cell to cell variation.

Conclusions Our characterisation of VSMC expression patterns showed both regional and local heterogeneity and suggested the presence of a subset of AA cells with a unique expression profile. These cells might be those responsible for the clonal proliferation we observed in disease[1], which would explain the AAs heightened plaque susceptibility. Our identified differentially expressed candidate genes may mark or regulate this population, aiding future investigations into the mechanisms underlying plaque development.

REFERENCES

1. Chappell, J. *et al*. *Circ Res* 2016;119:1313–1323.
2. Trigueros-Motos, L. *et al*. *ATVB* 2013;33:*1248*–1256.
3. Satoh, K. *et al*. *Circ Res* 2015;116:1098–1100.

208 CARDIOPROTECTION BY THE MITOCHONDRIA-TARGETED SUPEROXIDE GENERATOR MITOPARAQUAT IN A MURINE MODEL OF ACUTE MYOCARDIAL ISCHAEMIA REPERFUSION INJURY

[1]John Mulvey*, [2]Angela Logan, [2]Sabine Arndt, [1]Victoria Pell, [3]Stuart Caldwell, [3]Richard Hartley, [2]Michael Murphy, [1]Thomas Krieg. *[1]Department of Medicine, University of Cambridge*; *[2]MRC Mitochondrial Biology Unit*; *[3]WestCHEM School of Chemistry, University of Glasgow*

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Introduction Myocardial infarction is a major cause of death and disease worldwide. Mitochondrial reactive oxygen species