inflammatory genes and scavenger receptors, inducing an M2-like phenotype. Conversely, overexpression of miR-101 is associated with a pro-inflammatory phenotype (M1-like).

Conclusion miR-101-3p offers a potential target to simultaneously enhance the expression of ABCA1, MKP-1 and TRIB1, thus improving macrophage lipid metabolism and opposing inflammation, thereby attenuating atherosclerosis development.

Conflict of interest No

BS26

GENERATION OF A TISSUE ENGINEERED CONDUIT FROM HUMAN SAPHENOUS VEIN AND PORCINE BLOOD OUTGROWTH ENDOTHELIAL CELLS

Andrew Bond*, Nadiah Sulaiman, Vito Bruno, Jason Johnson, Sarah George, Raimondo Ascione. *University of Bristol*

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Introduction Coronary artery bypass grafting (CABG) primarily uses autologous human saphenous vein (hSV), despite autologous arteries having better patency rates. However, a lack of arteries, and presence of disease in those which are available, has led to the need to develop alternative tissue engineered conduits. Here we aim to arterialise a vein, by re-seeding a decellularised hSV (DhSV) with arterial-like endothelial cells (EC), which will ultimately prevent early thrombosis and improve late graft patency.

Methods Blood outgrowth EC (BOEC) isolated from 350 ml pig blood were expanded for further use. BOEC were subjected to immunocytochemistry (ICC) for EC markers CD31, vWF, VE-Cadherin, and DBA-Lectin, and also vimentin (mesenchymal/fibroblast marker) and CD45 (leukocyte marker). BOEC seeded in plates were exposed to dynamic (D) culture conditions on an orbital shaker (94 hrs) and compared to static (S) culture. EC isolated from pig aorta (PAEC) were used as positive controls. qPCR was performed for CD31, vWF, VE-Cadherin, eNOS, DLL4 (arterial) and NR2F2 (venous).

hSV was decellularised using 0.01% SDS. 1×10^6 BOEC were seeded onto DhSV by tying the ends (T) to trap cells lumenally, or placing BOEC in the lumen leaving ends untied (UT), before leaving under static (S) or dynamic (D: roller, 1rpm) culture conditions (93 hrs). Seeded DhSV were static cultured for 73 hours, fixed, paraffin wax-embedded and sections subjected to DBA-lectin staining to quantify maximum lumen coverage of BOEC, and anti-CD31 immunohistochemistry.

Results BOEC showed classic EC cobblestone morphology, and ICC staining revealed expression of CD31, DBA-Lectin, vWF, vimentin, VE-Cadherin levels were low and CD45 was not detected. CD31 mRNA levels were comparable in BOEC and PAEC (fold-change (FC) 1.2), while vWF (FC 228.3), VE-cadherin (FC 9.3) and NR2F2 (FC 5.5) mRNAs were increased and eNOS (FC 0.2) and DLL4 (FC 0.1) were decreased in BOEC compared to PAEC. Exposing BOEC to shear stress increased expression of all mRNAs investigated (FC CD31:2.6, vWF:1.8, VE-cadherin:1.4, eNOS:3.3, DLL4:1.4, and NR2F2:3.4) compared to static BOEC.

Seeding DhSV resulted in partial re-endothelialisation with greatest lumen coverage found by dynamic seeding with cells tied into lumen (91% coverage) and continued culture resulted in a near complete BOEC layer following (97%). CD31 was still expressed in seeded DhSV.

Conclusion BOEC isolated from pig blood show expression of EC markers, and vimentin, and are negative for the leukocyte marker CD45. We have shown that it is possible to repopulate a DhSV with BOEC and, under the correct conditions, obtain a functional monolayer around the lumen. This preliminary data shows the translational potential for this approach in generating a tissue engineered saphenous vein, reendothelialised with BOEC from blood that could be used for CABG.

Conflict of interest None

BS27

DEVELOPMENT AND PRECLINICAL TESTING OF A LARGE HEART MUSCLE PATCH

¹Richard Jabbour*, ¹Thomas Owen, ²Marina Reinsch, ¹Pragati Pandey, ¹Cesare Terracciano, ²Florian Weinberger, ²Thomas Eschenhagen, ¹Sian Harding. ¹Imperial College; ²Hamburg university

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Introduction The lack of efficacy of stem cell therapy for the treatment of heart failure may be related to the poor retention rates offered by existing delivery methods (intra-coronary/intramyocardial). Tissue engineering strategies improve cell retention in small animal models but data regarding engineered heart tissue (EHT) patches large enough for human studies are lacking.

Purpose To upscale EHT to a clinically relevant size and mature the patch in-vitro. Once matured to undergo preclinical testing in a rabbit model of myocardial infarction.

Methods We developed an upscaled EHT patch (3cm $\times$ 2cm $\times$ 1.5mm) able to contain up to 50 million human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CM) (figure 1A/B). Myocardial infarction model was performed by permanent ligation.

Results The patches began to beat spontaneously within 3 days of fabrication and after 28 days of dynamic culture (Late EHTs) showed the development of several mature characteristics when compared to early patches (<14 days from fabrication). For example, late EHTs contained hiPSC-CMs which were more aligned (hiPSC-CM accumulative angle change: early 2702 ± 778 degrees [n=4] vs late 922 ± 186 [n=5], $p=0.042$); showed better contraction kinetics (early peak contraction amplitude 87.9 ± 5.8 a.u. versus late 952 ± 304 a.u.; $p<0.001$) and faster calcium transients (time to peak: early 200.8 ± 8.8 ms [n=5] vs late 147.7 ± 10.2 ms [n=6], $p=0.004$; time to 75% decay: early 274 ± 9.7 ms vs late 219.9 ± 2.7 ms, $p=0.0003$).

We then tested the EHT patch in-vivo using a rabbit model (figure C). Patches were applied to normal (n=5) or infarcted hearts (n=8). Sham operations used non-cellular fibrin patches (n=5). The mean fraction of troponin positive cells in the graft was $27.8 \pm 10.3\%$ at 25.2 ± 1.7 days relative to day 0 [n=5] and KU80 (human specific marker) staining confirmed that this was of human origin. CD31 (figure D) and KU80 staining revealed that the grafts were well vascularized and that the vasculature was not human in origin (therefore were originating from the host). Ex-vivo optical mapping revealed evidence of electrical coupling between the graft and host at 2 weeks and preliminary experiments indicated that the patch improved left ventricular function when grafted onto infarcted hearts. Telemetry recordings in vivo and arrhythmia provocation protocols (ex vivo) indicated that the patch was not associated with any significant changes in arrhythmogenicity.