SARS ACADEMIC AND RESEARCH PRIZE: 0440: A COMPARISON OF THREE TENDON-TYING TECHNIQUES FOR USE DURING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION
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Aims: This study uses an animal model to examine the strength of three different suture-to-tendon attachment techniques for use during passage of hamstring graft through the tibial tunnel in ACL reconstruction.

Methods: Forty-eight fresh porcine anterior cruciate ligaments were fixed at one end. A suture was attached to the free end of each tendon using either a) Whipstitch b) Modified Prussik knot c) The Smith and Nephew Whipknot™device. The suture was loaded with 2.5N increments until structural failure. Load at failure and time taken to attach suture to tendon were recorded.

Results: Mean load at failure was 112N (standard deviation 9.7) for whipstitch, 111N (26.5) for modified Prussik, and 136N (15.9) for the Whipknot™. The Whipknot™ device was significantly faster than the Prussik knot technique (8.8s vs 15.8s, p<0.01), which in turn was faster than whipstitching (15.8s vs 121.5s, p<0.01).

Discussion: All three techniques provided sufficient strength for attaching a suture to the graft tendon during anterior cruciate ligament surgery. Whilst whipstitching is the most commonly used method, the modified Prussik technique can be recommended for its significantly shorter time for attachment. The Whipknot™ device, whilst both strong and fast, is more costly than the other two techniques.

SARS ACADEMIC AND RESEARCH PRIZE: 0696: MACROPHAGE MIGRATORY INHIBITORY FACTOR (MIF) SECRETION BY MESENCHYMAL STEM CELLS (MSC) AND COLORECTAL CANCER (CRC) CELLS IN 3-DIMENSIONAL CULTURE
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Aims: High serum MIF levels positively correlate with an increased risk of colorectal cancer metastasis in CRC patients. MSCs are multipotent stromal cells known to migrate into the tumour architecture. This study aimed to investigate interactions between MSCs and human CRC cells in three-dimensional culture.

Methods: Cultures were established of CRC cell lines (HCT-116/HT 29) and 136N (15.9) for the Whipknot™. The Whipknot™ device was significantly faster than the Prussik knot technique (8.8s vs 15.8s, p<0.01), which in turn was faster than whipstitching (15.8s vs 121.5s, p<0.01).

Discussion: All three techniques provided sufficient strength for attaching a suture to the graft tendon during anterior cruciate ligament surgery. Whilst whipstitching is the most commonly used method, the modified Prussik technique can be recommended for its significantly shorter time for attachment. The Whipknot™ device, whilst both strong and fast, is more costly than the other two techniques.

Conclusions: MIF was secreted by all cell populations examined, with the highest levels quantified and paraf- foci but not significantly altered when co-cultured with WI-38s. Upon co-culture, a net decrease in MIF secretion (21 –90% decrease) was observed. Interestingly, co-culture with WI-38s had the opposite effect, suggesting an MSC specific phenomenon.

Conclusions: This data highlights distinct effects of MSCs on the CRC tumour microenvironment. Considering the role of MIF in inflammation and the known link between inflammation and colorectal cancer, further investigation is warranted.

SARS ACADEMIC AND RESEARCH PRIZE: 0698: STATINS ENHANCE VEIN RECANALISATION AND REDUCE VEIN WALL INFLAMMATION FOLLOWING VENOUS THROMBOSIS
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Background: Statins exhibit anti-inflammatory, pro-angiogenic and pro-fibroinolytic effects that may affect thrombus recanalisation and organisation.

Methods: Venous thrombi were induced in BalbC mice by a combination of reduced flow and endothelial injury. On day-1, mice were randomised to 3 groups (n=7/gp). Atorvastatin (30mg/kg or 3mg/kg) or vehicle (methylcellulose) was given daily for 7 days by gavage. On day-7, thrombi were harvested and paraffin sections obtained at defined intervals. Vein recanalisation, thrombus volume, nucleated cell counts, macrophages (MAC-2) and neutrophils (NIMP-R14) content in the thrombus and vein wall were measured.

Results: Vein recanalisation was greater following high-dose Atorvastatin (0.50±0.13mm³) compared with low-dose or vehicle (0.29±0.11mm³, 0.27±0.13mm³, P=0.002 ANOVA). Neovascular channel number within the thrombus was significantly higher in both treated groups (5.0±±.44 high-dose); 5.1±.5 [low-dose], vs 3.1±±.40 [vehicle], P=0.009). Thrombus volume, nucleated cell count, MAC-2 and NIMP-R14 staining was similar for all three groups. Vein wall nucleated cell count was lower in treatment groups (637±74 [high-dose]); 649±75 [low-dose] vs control (1023±60, P=0.001). MAC-2 (0.41±±.04, 0.45%±±.04) and NIMP-R14 (3.92%±±.38, 3.76%±±.48) staining was significantly lower in the vein wall of statin treated groups compared with vehicle (0.97%±±.05, P=0.001; 7.33%±±.36, P=0.001).

Conclusions: Atorvastatin enhanced recanalisation and inhibited vein wall inflammation associated with wall fibrosis.

SARS ACADEMIC AND RESEARCH PRIZE: 0903: MIRNAS: SMALL MOLECULES, BIG PLAYERS IN TAMOXIFEN RESISTANCE IN BREAST CANCER
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Aim: The aim of this study was to identify and evaluate miRNAs that are dysregulated in tamoxifen resistance.

Methods: A microarray analysis was performed on lysates obtained from the MCF7 breast cancer cell line (ER+/PR+/HER2-). Parental MCF7 cells were cultured under estrogen deprivation (ED) conditions for 48 hours prior to short or long-term treatment with tamoxifen, estrogen or ED. Validation of microarray data was performed using RQ-PCR. Functional analysis of cell growth and apoptosis was performed following knockdown of miRNAs using in situ cell cytometry (Celigo).

Results: 58 out of 999 miRNAs were identified to be significantly altered across the various treatment and resistant groups (p<0.001). 23 miRNAs were observed to be upregulated and 41 downregulated in tamoxifen resistance. Microarray results were confirmed by RQ-PCR. A reduction in cell growth was observed in tamoxifen resistant cells following miR-1285 and miR-181c knockdown. Apoptosis was induced upon knockdown of miR-1285. Evaluation of predicted targets of miR-181c was performed using RQ-PCR.

Conclusion: This study has identified a number of miRNAs that are dysregulated in association with tamoxifen resistance in breast cancer, two playing a role in cell growth. Modulation of such miRNAs may offer novel therapeutic strategies in overcoming such resistance.

SARS ACADEMIC AND RESEARCH PRIZE: 1038 WINNER OF THE ASIT/ SARS ACADEMIC AND RESEARCH PRIZE: UNDERSTANDING THE DYNAMIC HAEMATOPOIETIC AND MESENCHYMAL STEM CELL CONTRIBUTION TO THE TUMOUR MICROENVIRONMENT OF CHOLANGIOCARCINOMA
Andrew Robson, Kay Samuel, Antonella Pellicoro, John Iredale, Stuart Forbes. University of Edinburgh, Edinburgh, UK

Background: Intrahepatic cholangiocarcinoma (ICC) is an aggressive malignancy of biliary epithelium with increasing global mortality. ICC is characterised by a pronounced inflammatory stroma of tumour-associated myofibroblasts, macrophages and immune cells. We aimed to define the stem cell source of these components.

Methods: Tumours were studied in humans and our thioacetamide (TAA) rat model of ICC. Bone marrow (BM) transplants were performed: ICC was then induced in sex-mismatched and GFP+ BM transplant recipients. Extra-hepatic derivation of cells was tracked over time using Y-Chromosome. The Smith and Nephew Whipknot™ device was significantly faster than the Prussik knot technique (8.8s vs 15.8s, p<0.01), which in turn was faster than whipstitching (15.8s vs 121.5s, p<0.01).

Discussion: All three techniques provided sufficient strength for attaching a suture to the graft tendon during anterior cruciate ligament surgery. Whilst whipstitching is the most commonly used method, the modified Prussik technique can be recommended for its significantly shorter time for attachment. The Whipknot™ device, whilst both strong and fast, is more costly than the other two techniques.

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