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The Association of Surgeons in Training Conference Abstracts

ASIT MEDAL: 0311: OESTROGEN RECEPTORS AND OESOPHAGEAL CANCER: A POTENTIAL THERAPEUTIC PATHWAY

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Introduction: Oestrogen receptors (ER) have a well-established link in the initiation, progression and response to treatment of some cancers. Little is known, however, about the significance of ER as therapeutic biomarkers in oesophageal cancer (OC).

Methods: Effects of ER modulators on proliferation in OE33 and OE19 OC cells was evaluated. ERα and ERβ expression in paired normal and tumour oesophageal samples ($n = 34$) was performed using RT-qPCR. Correlation between ER mRNA expression and clinico-pathological features for OC was determined.

Results: There was a significant dose dependent inhibition of proliferation in OE33 and OE19 OC cells by a highly selective ERα antagonist (MPP) and an ERβ specific antagonist (PHTPP) ($p < 0.05$). RT-qPCR analysis revealed that ERα and ERβ mRNA expression was significantly higher ($p<0.05$) in tumour tissues relative to their paired normal mucosa. Expression of ERα and ERβ in tumour samples correlated inversely with survival outcome ($p<0.05$). Up-regulation of ERα correlated with higher pathological T stage ($p<0.05$) and lymph node metastasis ($p<0.05$), while ERβ up-regulation correlated with positive vascular invasion ($p<0.05$).

Conclusions: Our findings indicate a role for ER in the biological behaviour of OC. Hence, the ER system may provide an additional novel target for the treatment of OC.

ASIT MEDAL: 0853: ASIT ANSELL MEDAL PRIZE WINNER: HUMAN AMNIOTIC EPITHELIAL CELLS MODULATE ALLOREACTIVE T-CELL ACTIVITY: A POTENTIAL ADJUNCT TO CELLULAR TRANSPLANTATION

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Introduction: Human amniotic epithelial cells (AEC) display immunomodulatory properties. We have previously demonstrated that bio-engineered transplantable constructs formed by co-culturing human islets and AEC (islet:AEC) exhibit markedly reduced immunogenicity in contact with peripheral blood mononuclear cells (PBMC) compared to unmodified islets, which is likely to reduce their vulnerability to graft rejection. To extend these findings we now provide evidence that distinct T-cell subpopulations, implicated in allograft destruction, are targets for AEC immunomodulation.

Methods: Magnetic assisted cell sorted CD4+ and CD8+ T-cells were cultured alone or in contact with human AEC, islets or islet:AEC constructs, using CD3/CD28 to induce physiological activation and expansion. The degree of allo-reactivity viz. T-cell proliferation was assessed by chemiluminescence assay.

Results: CD4+ and CD8+ T-cell proliferation was responsive to AEC co-culture with CD3/CD28 activation being dose-dependently reduced ($p<0.05$). CD4+ and CD8+ proliferation was also markedly attenuated on contact with islet:AEC constructs compared to that observed with unmodified islets ($p < 0.05$).

Conclusion: T-cells that are known to mediate allograft rejection in cell transplantation are modulated by AEC. AEC may therefore serve as an adjunct in cell transplantation, reducing the requirement for chronic systemic immunosuppression and promoting long-term graft survival.

ASIT MEDAL: 0921: PROSPECTIVE STUDY TO ASSESS TUMOUR NECROSIS FACTOR ALPHA IN NON-INFLAMMATORY BOWEL DISEASE ENTEROCUTANEOUS FISTULA

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Aim: Tumour necrosis factor alpha (TNF-α) is elevated in inflammatory bowel disease enterocutaneous fistula (IBD ECF). No study has assessed the level in non-IBD ECF. The aim of this study was to assess the inflammatory activity, with a particular emphasis on TNF-α in non-IBD ECF when compared with control small bowel tissue.

Methods: Tissue biopsies were obtained from ECF at operation from non-IBD patients and from normal control patients. After overnight culture, intracellular staining was performed using monensin to assess on-going production of TNF-α. Data was acquired using FACS Canto II. Unpaired Student's t-test was used to compare variables between groups.

Results: The on-going production of TNF-α from dendritic cells ($p = 0.0007$), putative monocyte and B cell populations ($p = 0.04$) and CD3+ T cells ($p = 0.04$) was significantly higher than that from control tissue.

Conclusions: This study reveals encouraging results and may provide evidence for the potential use of anti-TNF-α agents in the treatment of non-IBD ECF. Recommendations are for a pilot study to assess whether this can be an alternative option to benefit an already surgically challenging group of patients. Positive findings would equate to a major medical advance with a new use for anti-TNF-α agents.

ASIT MEDAL: 1281: A NOVEL NEAR INFRARED EMITTING FLUORESCENT NANOPARTICLE FOR SENTINEL LYMPH NODE BIOPSY

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Background: Quantum dots (QDs) are fluorescent nanoparticles with unique photophysical properties that can potentially replace the current tracers for Sentinel Lymph Node Biopsy (SLNB) including the blue dye and radiocolloid that have various limitations. Near Infra Red (NIR) emitting QDs can be tracked in deep tissues as biological tissues are transparent to these wavelengths. We have developed NIRQDs as alternative probes for SLNB and set up a live NIR imaging system to track them in vivo.

Materials & Methods: NIRQDs (CdTe/CdS/ZnSe) were synthesized and characterized using various techniques. 100μL of QDs were co-injected with blue dye into the hind legs of rat models (n=4) and compared to controls (n=4) which were injected with blue dye only. QDs were tracked using a live NIR imaging system that was set up in house.

Results: NIRQDs emitted at 720nm and were visualised by the live NIR imaging system as they entered the lymphatics after injection. The lymphatics converged to the groin and a small surgical incision at this site revealed the underlying sentinel lymph node with minimal dissection.

Conclusion: NIR emitting QDs can be used for accurate localisation of the SLN prior to surgical incision, making this an even more minimally invasive procedure.

ASIT MEDAL: 1344: ISOLATED LIMB PERFUSION WITH MELPHALAN, TNFA AND ONCOLYTIC VACCINIA VIRUS DELAYS TUMOUR GROWTH AND PROLONGS SURVIVAL IN A RAT MODEL OF LOCALLY-ADVANCED EXTREMITY SARCOMA

Tim Pencavel [1], Rohit Seth [2], Aadil Khan [2], Michelle Wilkinson [1], Andrew Hayes [1], Kevin Harrington [2]. [1] *Sarcoma/Melanoma Unit, Royal Marsden Hospital, London, UK;* [2] *Targeted Therapy Team, The Institute of Cancer Research, London, UK.*

Aim: Isolated Limb Perfusion (ILP) is used for extremity sarcoma and in-transit melanoma. Adding oncolytic viruses may improve the efficacy of both treatments, and raises the possibility of locoregional therapy priming a systemic immune response.

Preclinical studies were performed to establish: feasibility of the model; additional therapeutic effect of Vaccinia virus (VV); and preclinical data to support a clinical trial.

Method: In vitro assays quantified single-agent and combinatorial activities of melphalan, TNFα and VV against sarcoma and melanoma cells. An immunocompetent rat extremity sarcoma model was developed to evaluate tumour response, survival, biodistribution and toxicity of VV.

Results: The combination of melphalan/VV was synergistic in vitro. Triple-therapy ILP was well tolerated, and resulted in prolonged survival and tumour growth delay in both microscopic and established tumour models compared to doublet, by 50% in established tumours (24 vs 16 days, p=0.0001). Virus was recoverable from perfused regions, and titres recovered indicated successful viral replication.

Conclusions: The addition of VV to TNFα/Melphalan ILP regimens increases survival. No extra morbidity occurred as a result. Normal organs were not infected. A Phase 1 trial of VV by ILP is undergoing ethical and regulatory scrutiny, with the aim of commencing recruitment in 2013.

ASIT MEDICAL STUDENT PRIZE: 0215: ASIT/ELSEVIER MEDICAL STUDENT PRIZE WINNER: A COMPARATIVE STUDY USING ULTRASOUND (US) AND CLINICAL PALPATION TO EVALUATE EASE OF VASCULAR ACCESS WITH DIFFERENT PELVIC BINDERS IN HEALTHY VOLUNTEERS

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Background: Mortality from haemorrhage associated with pelvic ring injuries remains high. Immediate application of a pelvic binder is a crucial step in damage control resuscitation (DCR) for these patients. Therapeutic angiography is a further effective intervention for managing arterial haemorrhage and the Common Femoral artery (CFA) is the preferred site for vascular access.

Aim: To determine which binder design provides greatest access to the femoral vessels for therapeutic angiography in a group of healthy volunteers.

Method: Four different binders, the T-POD, SAM-Sling, Prometheus and Improvised binder were applied correctly to fourteen volunteers. Access to the femoral vessels was assessed by attempting to palpate the femoral pulse, and by using US, performed by a consultant radiologist, to determine whether the CFA and Superficial femoral artery (SFA) were detectable and their depth. Volunteer Body Mass Indices were also recorded.

Results: Successful palpation of femoral pulse: SAM-Sling 57%, T-POD 7%, Promethus 29% and Improvised binder 36%. CFA identified on US: SAM-Sling 43%, T-POD 0%, Promethus 0%, and Improvised binder 29%. SFA identified on US: SAM-Sling 64%, T-POD 100%, Promethus 100% and Improvised binder 71%.

Conclusion: The SAM-Sling and Improvised binder allowed better access to the CFA, in both normal and overweight individuals.

ASIT MEDICAL STUDENT PRIZE: 0364: THE USE OF SYMNOSE FOR THE QUANTITATIVE ASSESSMENT OF LIP SYMMETRY FOLLOWING REPAIR OF COMPLETE BILATERAL CLEFT LIP AND PALATE

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Aim: The SymNose computer program has been proposed as an objective method for the quantitative assessment of lip symmetry following unilateral cleft lip repair. This study aims to demonstrate the use of SymNose in patients with bilateral complete cleft lip and palate (BCLP), a group previously excluded from computer-based analysis.

Method: A retrospective cohort study compared several parameters of lip symmetry between BCLP cases and non-cleft controls. 15 BCLP cases aged 10 (±1 year) who had undergone primary repair were recruited from the patient database at the South West Cleft Unit, Frenchay. Frontal facial photographs were selected for measurement. 15 age-matched controls were recruited from a local school. Lip symmetry was expressed as: percentage mismatch of left vermillion border and upper lip area over the right, horizontal lip tilt and lateral deviation of the lip.

Results: A significant increase in lip asymmetry was found in the BCLP group expressed as upper vermillion border mismatch across computer-defined and user-defined midlines (mean difference was 16.4% ($p<0.01$) and 17.5% ($p<0.01$) respectively).

Conclusions: The results suggest that a significant degree of lip asymmetry remains in BCLP patients even after primary repair. This challenges previous assumptions that those with bilateral defects would be relatively symmetrical.

ASIT MEDICAL STUDENT PRIZE: 0433: PAIN AFTER TOTAL KNEE REPLACEMENT (TKR). A RANDOMISED CONTROLLED TRIAL OF LOCAL INFILTRATION VERSUS SINGLE SHOT FEMORAL NERVE BLOCK

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Background: Multiple modalities can be used to manage pain after TKR. There are no studies of local joint infiltration versus single shot femoral nerve block.

Objectives: We conducted an ethically approved prospective blinded randomised trial. We aimed to identify whether local infiltration gave better postoperative pain relief compared to standard practice of single shot femoral nerve block.

Methods: 40 patients undergoing a primary TKR underwent a standardised spinal anaesthetic and where then randomised to one of two groups. Outcomes measured included postoperative pain scores, pain scores before and after physiotherapy on postoperative day 1, analgesia used postoperatively, time to achieve physiotherapy goals and length of hospital stay.

Results: The local infiltration group had significantly lower pain scores postoperatively (mean [SD] 2.1[2.6] vs 6.8[3.2], $p<0.0001$) and on postoperative day one prior to physiotherapy (mean [SD] 2.9[2.3] vs 4.4[2.3], $p<0.05$). Total opiate use was significantly lower in the infiltration group