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Abstracts

Proceedings of the second annual Queen's University Belfast Student Research Symposium

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OVERVIEW

On the 12th November 2014, the Queen's University Academic Medicine Society (QUAMS) convened the second annual Student Research Symposium at Riddel Hall. The meeting was organised in collaboration with staff from the School of Medicine, Dentistry and Biomedical Sciences, had over 100 registered delegates and funded by a £10,000 INSPIRE grant from the Academy of Medical Sciences.

The conference was the second conference to engage with medical and dental students from across all year groups and empower them to put forward abstracts to present as oral and poster presentations. A keynote speech by trainee surgeon Mr Edward Fitzgerald, concerned student engagement with research with tips and tricks for students to get their foot in the door. The event also brought together academic leads from the School of Medicine, Dentistry and Biomedical Sciences Intercalated Degree and Summer Studentship programmes.

28 students submitted abstracts to the conference on a wide variety of topic areas and backgrounds. Some of the topics included surgical admission rates, female genital mutilation in low and middle income countries as well as cystic fibrosis and nerve degeneration. All 28 students were offered the opportunity to present with 6 selected for oral presentations. Judges were present to assess all the students who presented with a winner and runner-up selected from each category of presentation. The winning abstracts are detailed below with the student indicated by a ** in each case.

The conference organisers are incredibly grateful for all the help received from staff in the university and hope to see as many students as possible for the 2015 Student Research Symposium next academic year. For more information about QUAMS and the symposium, please go to www.quams.org.uk.

ORAL PRESENTATION- WINNER

"The impact of pre-pregnancy care on pregnancy planning indicators in pregnancy complicated by diabetes mellitus"

Meghan Deery[1], Lesley Hamill[1], David R McCance[2], Michelle Spence[3], Fiona Alderdice[4], Roy Harper[5], and Valerie A. Holmes[1]

Background: Women with diabetes are at increased risk of adverse pregnancy outcomes compared to the background maternity population. Pre-pregnancy care (PPC) constitutes specialised medical care provided for women with diabetes which reduces adverse pregnancy outcomes. Two thirds of women in the Confidential Enquiry into Maternal and Child Health received suboptimal PPC[1]. This study evaluates the provision and impact of self-reported and optimal PPC in Northern Ireland (NI).

Methods: Data on PPC was collected during patients' first visit to a specialist antenatal-metabolic clinic as part of a regional service evaluation of the integration of a preconception counselling resource into routine care in NI. 'Optimal PPC' was defined according to NICE Guidelines. Women who reported receiving PPC were compared to those who did not receive PPC. Women categorised as receiving 'optimal PPC' were compared to those who received suboptimal or no PPC.

Results: 129 women attended clinics over a 12 month period. 80% (n=103) of women reported receiving PPC, with 38% (n=54) categorised as having received optimal PPC. Women who reported receiving PPC and those who received 'optimal PPC' had significantly lower HbA1c at their first clinic visit (56.4mmol/mol vs 64.1mmol/mol, P=0.032 and 51.4mmol/mol vs 63.3mmol/mol, P<0.001, respectively).

Conclusion: Two thirds of women who reported receiving PPC did not receive optimal care, highlighting a discrepancy between how women perceive PPC and current best practice. Both self-reported and optimal PPC were associated with improved glycaemic control, with optimal care having a greater impact. Further efforts are needed to ensure that all women with diabetes receive optimal PPC.

Footnote

1. Confidential Enquiry into Maternal and Child Health (2007) Diabetes in Pregnancy. Are we Providing the Best Care? Findings of a National Enquiry: England, Wales and Northern Ireland London: CEMACH

ORAL PRESENTATION- RUNNER-UP

"Investigating the clinical potential of induced pluripotent stem cell-derived endothelial cells in wound healing"

Philip McCaughey, James Bojdo, Christina O'Neill, Jasenka Guduric-Fuchs, Sophia Kelaini, Reinhold Medina, Sandra McAllister, Andriana Margariti, Alan Stitt

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Background: Following cutaneous injury, timely restoration of integumental integrity is essential to restore homeostatic conditions. Revascularization is a critical process in wound healing; however conditions associated with defective endothelial function and repair, such as diabetes, impair this process, leading to the development of chronic wounds. Studies have shown that endothelial progenitor cells (EPCs) have an important role in physiological tissue repair and regeneration, but these cells can be difficult to isolate and become senescent relatively quickly in culture. Therefore, translation to clinical use may be problematic. Induced pluripotent stem cells (iPSCs) offer promise as an alternative source of proliferative cells from which endothelial-like cells may be generated. Methods: Induced pluripotent stem cells (iPSCs) were generated from human fibroblasts via a DNA-free integration method over a period of 28 days. Endothelial differentiation was achieved by seeding cells on collagen IV-coated dishes in EGM-2 medium supplemented with vascular endothelial growth factor, following which cells were selected for either CD34 or KDR - known vascular progenitor markers. Three-dimensional cultures were performed to investigate the potential to produce implantable microvascular networks.

Results: iPSCs were successfully generated from human fibroblasts and subsequently differentiated into proliferative, endothelial-like cells (iPSC-ECs) capable of forming microtubular networks in collagen scaffolds in vitro. In addition, a number of novel genes implicated in the processes of endothelial differentiation and angiogenesis were found to be upregulated.

Conclusion: This work demonstrates that it is possible to generate iPSC-ECs from adult human fibroblasts. iPSC-ECs had similar characteristics to EPCs and have considerable potential for clinical use as personalised, cell-based therapy.

POSTER PRESENTATION- WINNER

"Induction of zinc finger protein A20 in Cystic Fibrosis: Investigating compounds with anti-inflammatory action"

Beth Malcomson[1], Shu-Dong Zhang[2], Madeleine Ennis[1] and Bettina C Schock[1]

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Background: Various CFTR gene mutations lead to sticky mucus production throughout the body in Cystic Fibrosis (CF) patients. Bacterial colonisation in airway epithelium leads to chronic inflammation and tissue damage, exacerbated by faulty regulation of the innate immune response that can ultimately lead to respiratory failure. In the Toll Like Receptor 4 (TLR4) signalling pathway that contributes to this response against Gram negative bacteria, the protein A20 negatively regulates Nuclear Factor-κB. In turn this is responsible for the release of the pro-inflammatory cytokine, IL-8.

In CF a lack of A20 contributes to the hyperinflammatory phenotype of the airway epithelium. Connectivity Mapping has been successful to predict licensed cancer drugs that can modify the expression of a given target gene. We hypothesise that Connectivity Mapping can be used to predict drugs that exert an anti-inflammatory effect in primary nasal epithelial cells (PNECs) by up-regulation of A20. The study investigated the effects of the predicted drugs (one positive, one negative) on A20 mRNA expression and LPS induced IL-8 release.

Methods: Using 6 independent GEO databases of 81 samples of epithelial cells from CF and non-CF subjects, linear regression analyses were applied to A20 correlates to create a gene signature. The predicted A20 inducing drugs include Azoclonol, Ikarugamycin, and Quercetin but Fluvastatin was predicted not to induce A20. Non-CF and CF (F508del homozygous) PNECs were pre-treated for 1h with Fluvastatin (0.1, 1μM), Quercetin (0.1, 100μM) and Dexamethasone (1μM) followed by stimulation with lipopolysaccaharide (LPS 10ug/ml for up to 24h).

Results: LPS induced IL-8 release determined by ELISA (PeproTech) in the 24h supernatant was significantly reduced in CF PNECs with Fluvastatin pre-treatment ($p<0.05$) at 0.1 and 1 μM and in non-CF PNECs at 1 μM ($p<0.05$), confirming previous findings in CFBE41o- and 16HBE14o- cell lines. With Quercetin pretreatment LPS induced IL-8 release was decreased without statistical significance at 0.1 μM (n=4). Total RNA was extracted and reverse transcribed into cDNA for qPCR analyses of A20 mRNA. Fluvastatin pre-treatment (with and without LPS stimulation) did not induce A20 at any concentration, Quercetin in line with the hypothesis shows A20 up-regulation at some time points but to date only non-CF PNECs (n=3) have been analysed.

Conclusion: Connectivity Mapping can successfully predict drugs from a list of already licensed drugs to induce A20. Some of these drugs may be repositioned as anti-inflammatory for CF patients with chronic airway inflammation.

POSTER PRESENTATION- RUNNER-UP (JOINT PRIZE)

"Identification of inflammasome expression in EAE"
Samara Fleville- Abstract not published here

"Preliminary assessment of the expression and release of soluble endoglin in cultured human placental trophoblasts

under hypoxic and diabetic stresses"

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Introduction: Preeclampsia (PE), manifested as new-onset hypertension and proteinuria occurring after 20 weeks of gestation, remains a major cause of morbidity and mortality in pregnancy. Women with diabetes are at a greatly higher risk of developing PE (15-30% vs. 3-5% in general population). It is believed that maternal vascular symptoms are mediated by an abnormally increased release of anti-angiogenic factors such as soluble endoglin (sEng) from the placenta, possibly due to hypoxia. We previously found that the presence of pre-gestational diabetes raises blood levels of sEng during the second half of gestation, which may contribute to the higher incidence of PE in these women.

Objective: To determine if the expression and release of sEng can be modulated by hypoxia and diabetic conditions in a common human trophoblast cell line.

Methods: Cultured BeWo choriocarcinoma cells were treated with stresses simulating PE (hypoxia) and diabetes (high glucose, 'heavily glycated, oxidized LDL') for 24-48 hours. Expression of endoglin was quantified by RT-PCR in cell lysate, and sEng was measured in supernatant by ELISA.

Results: Hypoxic treatment enhanced cellular expression of endoglin at the mRNA level, but appeared to reduce its protein release in supernatant when compared to normoxia. Levels of sEng in supernatant were not affected by high glucose, but were decreased by modified vs. native LDL.

Conclusion: In this preliminary exploration, we found that hypoxia and diabetes-relevant stresses altered the expression and release of sEng in cultured BeWo trophoblast cells. Further investigation is needed to confirm the observation, and to understand the mechanisms.