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Abstracts

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

Wednesday 11 April 2018, Wellcome-Wolfson Institute for Experimental Medicine

OVERVIEW

QUB SCRUBS hosted the Student Research Symposium providing a forum for medical and dental students across all year groups to present research conducted during student summer studentships and intercalated degrees. Twenty students submitted abstracts for poster or oral presentations. Speakers at the symposium included Professor Peter Maxwell, Clinical Academic Training Programme director and Dr Michael Corr, Academic Foundation Year 2 trainee. The three prize winning abstracts were presented by medical students Ger Mullan, Sinead Donnelly and Dharsshini Reveendran. The symposium was organised in collaboration with staff from the School of Medicine, Dentistry and Biomedical Sciences and was made possible by support from Queen's University Belfast, the Medical Defence Union and the Wesleyan company.

FIRST PRIZE

Inflammasome Expression in Healthy and Diseased CNS

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Background: Damaged and foreign material pose a threat to our body. The innate immune system can recognise these 'danger signals' and rapidly mount a response to eliminate that threat. Sensing danger causes the formation of the inflammasome, which generates and releases pro-inflammatory cytokines interleukin-1β (IL-1β) and interleukin-18 (IL-18) out of the cell. These cytokines stimulate the innate and adaptive immune response to the threat.

Inflammasomes are thought to be involved in Multiple Sclerosis (MS). MS is a chronic demyelinating disease that can cause serious neurological disability, often leaving patients wheelchair-bound within 20 years of diagnosis. Experimental autoimmune encephalomyelitis (EAE) is a mouse model used to study MS pathology.

The aim of this study was to characterise and compare the expression of inflammasomes in both healthy and diseased CNS in mouse models of MS.

Methods: Spinal cords were perfusion-harvested from adult healthy and EAE C57BL/6 mice. 14µm sections were prepared using a Leica CM1950 Cryostat. Sections were immunofluorescently stained for inflammasome markers such as AIM2 and NLRC4, and imaged using a Leica DMi8 inverted epifluorescent microscope.

Results: AIM2 is expressed in healthy CNS in both grey and white matter, however, expression was low and scarce, whereas NLRP3 is not expressed in healthy CNS. In contrast, inflammasome proteins such as AIM2 and NLRC4 are highly expressed in EAE tissue. Interestingly, NLRC4 is differentially expressed in white and grey matter in both healthy and diseased spinal cord tissue.

Conclusions: This work demonstrates differential expression of inflammasomes that may correlate with the role of inflammasomes in healthy and diseased CNS. Future work will involve identifying the role of inflammasomes in CNS homeostasis and demyelination using a lysolecithin-induced disease model, which allows distinguishing between stages of demyelination and remyelination.

Acknowledgements: This study was funded by grants to YD (the Royal Society, the Fritz-Thyssen Foundation, the Leverhulm Trust).

SECOND PRIZE

The role of the Glucocorticoid Receptor (GR) in Triple Negative Breast Cancer (TNBC) in response to DNA damaging chemotherapy treatment

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Background: Triple negative breast cancer (TNBC) is a type of breast cancer that does not express the oestrogen receptor (ER), the progesterone receptor (PR) and does not have amplification of the human epidermal growth factor receptor 2 (HER-2). It is an aggressive form of breast cancer which has poor clinical outcomes. Currently, the standard of care for TNBC patients is DNA damaging chemotherapy, which has a variable response rate. This study aims to evaluate the role of

the androgen receptor (AR) and the glucocorticoid receptor (GR) in TNBC, and their ability to modulate DNA damaging chemotherapy and anti-microtubule agents.

Methods: GR expression was evaluated through in silico analysis using in house and external data sets. TNBC cell lines were modulated, using both siRNA (ARsi and GRsi) and pharmacological modulation (GR agonist Dexamethasone GR antagonist Mifepristone, AR antagonists Bicalutamide and Enzalutamide). Statistical analysis was carried out using Prism 5.

Results: *In silico* analysis showed that high GR expression was associated with improved clinical outcome versus patients with low GR expression. In TNBC cell lines treated with DNA damaging agents, the GR agonist Dexamethasone increases sensitivity to chemotherapy. Dexamethasone is used to attenuate chemotherapy related side effects in TNBC patients, and may therefore be modulating response. Conversely, in TNBC cells treated with anti-microtubule agents, Dexamethasone decreased sensitivity to chemotherapy.

Conclusions: This study recommends that TNBC patients receiving DNA damaging chemotherapy may benefit from the addition of Dexamethasone. Those receiving anti-microtubule agents should be given an alternative anti-emetic, as Dexamethasone reduced sensitivity to this chemotherapy.

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THIRD PRIZE

Do nutrient and health claims have an impact on the perceived healthiness and the amount of food/meals eaten by adults on the island of Ireland? An experimental breakfast study

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Background: A previous study has demonstrated that when people thought they were eating a low-calorie milkshake (versus a high-calorie labelled equivalent though same product) their physiological satiety, as measured by the gut peptide ghrelin, was consistent with what they believed they were consuming rather than the actual nutritional value (Crum et al., 2011). If replicated and shown for different food types this finding could have implications for nutrient and health claims labelling and advertising. The aim of the current study was therefore to replicate this experiment using a different type of food.

Methods: On two separate occasions, with an interval of one week in between visits, participants (N=50) were asked to consume a 380 calorie yoghurt and granola breakfast product under the pretence that it is either a 500 calorie 'indulgent' breakfast (high in fat and sugar) or a 250 calorie 'sensible' breakfast (low in fat and sugar).

At each visit blood samples were collected at three time-points to measure acylated ghrelin: after a 20-minute rest period (baseline), after 60 minutes (anticipatory) and after 90 minutes (post-consumption). Participants were asked to complete self-reported appetite measures (visual analogue scales) 10 minutes prior to each blood sample. During the first interval (between 20 and 60 minutes) participants were asked to rate the breakfast label based on its appearance and perceived healthiness, and during the second interval (between 60 and 90 minutes) participants were instructed to consume the breakfast product in its entirety within 10 minutes while rating the breakfast's sensory appeal.

Results : From anticipatory to post-consumption participants reported a significantly higher mean change in self-reported fullness score (i.e. feel fuller) for the 'indulgent' breakfast than the 'sensible' breakfast (mean change difference: 7.19 [95% CI: -0.73, 13.6]; P = 0.030). This relationship was not observed between baseline and post-consumption time points, or for the other self-reported appetite measures (hunger, satiety, quantity could eat and desire strength to eat) at any of the time points. Mean change in acylated ghrelin was not significantly different between the breakfasts at any of the time points.

Conclusions: This experimental study demonstrated an increase in self-reported fullness after consuming the 'indulgent' breakfast compared to the 'sensible' breakfast. A physiological response, however, was not observed as mean change in acylated ghrelin was not significantly different between the breakfasts.

Acknowledgements: This study was funded by Safefood

Fig 1. SCRUBS Research Symposium Prize winners (L-R) Dharsshini Reveendran, Ger Mullan and Sinead Donnelly.