PLYMOUTH UNIVERSITY PENINSULA

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CARDIFF UNIVERSITY PRIFYSGOL CAERDYDD

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The Academy of Medical Sciences

National Intercalators' Research Conference 2015

INSPIRE National Intercalators' Research Conference

Lecture Theatre 1 & 2

School of Chemistry
University of Bristol
Cantock's Close
Bristol, BS8 1TS

Saturday 24 October 2015
09:30 – 18:30

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Introduction

It gives us great pleasure to welcome you to the first **INSPIRE National Intercalators' Research Conference** hosted in Bristol on behalf of the Universities of Bristol, Cardiff, Exeter and Plymouth.

The **INSPIRE** initiative, led by the Academy of Medical Sciences (and supported by The Wellcome Trust), aims to engage students with research. Historically intercalated science degrees, embedded within professional training programmes, have been a key turning point in the careers of many clinical academics. There are many pressures on students today but encouragingly intercalation remains popular. Through this conference we hope to celebrate the achievements of recent intercalators and give insights as to the opportunities available to clinical students.

Our conference is open to Medical, Veterinary and Dental students nationwide and has twin objectives:

- To provide a peer reviewed scientific forum for the presentation of research undertaken by intercalating students.
- To offer students considering intercalation the opportunity to obtain information about their options and to speak to programme leads and to past students

The conference will feature:

- Presentations selected for Oral presentations
- Facilitated poster discussion session
- With prizes for each category (voted for by the delegates)
- Stands and short talks from intercalation programme leads
- A keynote address from Dr Tony Pickering, Wellcome Trust Senior Clinical fellow and Consultant Anaesthetist, Bristol
- Talks from more junior professionals on how intercalation has influenced their subsequent career tracks.
- We will also facilitate networking at lunch and post-conference wine tasting.

With over 170 students attending and 18 oral plus 40 poster presentations, this is shaping up to be an excellent conference. We look forward to seeing you in Bristol.

Programme Overview

Time		
9:30	Registration and coffee	
10:00 10:15	Welcome to conference Prof George Banting - Dean, Faculty of Biomedical Sciences	
10:15 10:45	Keynote lecture: Dr Tony Pickering (Anaesthetist & Wellcome Senior Clinical Fellow, Bristol) **"A career set in oscillation..."**	
11:00 12:30	**Intercalators' Research Presentations** (6 x 10+5 mins)	
	Theme 1: **Cancer, Immunology & Infection**	Theme 2: **Cardiorespiratory, Endocrine & Neuroscience**
12:30 14:00	Lunch and poster session + Intercalation programme fair	
14:00 15:30	Research presentations Theme 3: **Epidemiology, GP and Global Health**	**Intercalation programme talks**
15:30 16:00	Coffee / Tea break	
16:00 17:00	**Workshop: "My career after intercalation"** (4 x talks)	
17:00 17:15	Meeting close and prize awards Prof Jonathan Sandy, Dean of Faculty of Health Sciences	
17:15 18:30	Wine, nibbles & networking	

Detailed Schedule

09:30 Registration and Coffee

10:00 Welcome to Conference **(Theatre 1)**
Professor George Banting, Dean of The Faculty of Biomedical Sciences

10:15 Keynote Lecture by: **(Theatre 1)**
Dr Tony Pickering, Wellcome Senior Fellow & Anaesthetist, Bristol
"A career set in oscillation..."

11:00 - 12:30

Intercalators' Research Presentations

Theme 1: **Cancer, Immunology and Infection** **(Theatre 2)**

Chair: Linda Wooldridge

Oral Presentations by:

11:00 1 **Bethany Kingston**, Oxford University
The Role of the Transcription Factor ZBTB1 in Lymphocyte Development

11:15 2 **James Sun**, Cambridge University
A novel inhibitor of necroptosis in human breast and mouse mammary cell

11:30 3 **Natasha Daoud**, University of Bristol
The Role of Platelets and TGF-B in Prostate Epithelial and Cancer Cell Migration

11:45 4 **Nathan Jenko**, University of Oxford
The correlation between T-cell receptor ligand affinity and T-cell activation at supraphysiologic affinities

12:00 5 **Amy Hodgkiss**, University of Bristol
The effect of Lrg1 on vascular integrity in uveitis

12:15 6 **Ikhuemose Ikhena**, University of Oxford
Functional Characterisation of a Regulatory Variant Associated with Rheumatoid Arthritis in the MHC Class II

Detailed Schedule

Theme 2: **Cardio-respiratory, Endocrine and Neuroscience (Theatre 1)**

Chair: Elizabeth Coulthard

Oral Presentations by:

11:00 7 **Samuel Simpson**, Sheffield University
Expression analysis and knockdown of the novel MS-causing gene GRAMD1B during zebrafish development

11:15 8 **Natalie Lewis**, Cardiff University
Investigating whether the invasive respiratory pathogen Aspergillus fumigatus can evade innate immune recognition

11:30 9 **Anuriti Aojula**, University of Birmingham
Decorin reduces communicating hydrocephalic pathology: a diffusion tensor imaging and immunohistochemical study

11:45 10 **Cian Wade**, Year, University of Oxford
Post-movement beta activity in sensorimotor cortex indexes confidence in estimations from internal models

12:00 11 **Jonathan Chuo Min Lee**, University of Bristol
The Role of Group II metabotropic glutamate receptors in the cornu ammonis 2 region of the hippocampus

12:15 12 **Joe Finney**, Cardiff University
Studying the re-innervation of dopaminergic neurons in a zebrafish model

12:30-14:00 **Lunch, Poster Session & Intercalation programme stands**

Including @ 13:00 **Facilitated Poster discussion**
(Facilitators: Richard Coward, David Parkinson and Joanna Tarr)

Detailed Schedule

14:00 - 15:30

Intercalators' Research Presentations

Theme 3: Epidemiology, General Practice and Global Health (Theatre 2)

Chair: Colin Dayan

Oral Presentation by:

14:00 13 **Georgina Prestwich**, University of Bristol
Menstrual hygiene management amongst schoolgirls in Uganda and the impact on their education: a cross sectional study

14:15 14 **Rob Ayres**, Final Year, University of Southampton
Omega-3 long chain polyunsaturated fatty acids in human health: a link between obesity and status?

14:30 15 **Elizabeth McGeorge**, University of Birmingham
Incidence and spectrum of health problems and health service utilisation among backpackers in Thailand

14:45 16 **Georgina Frew**, University of Birmingham
Hepatitis B: knowledge, attitudes and practices amongst backpackers in Thailand

15:00 17 **Sarah Johnson**, Cardiff University
Model to investigate the relative effects of auditory and visual distractions in an operating theatre environment

15:15 18 **Niall McCartan**, University of Liverpool
The impact of an educational intervention on patient assessment and communication skills in escalation of care.

Detailed Schedule

14:00 - 15:30

Intercalation Programme Talks **(Theatre 1)**

Chair: David Dymock/Eugene Lloyd

14:00 **Helen Kennedy, University of Bristol**
Neuroscience (BSc), Pharmacology (BSc), Physiological Science (BSc)

14:10 **Liang Fong-Wong**, University of Bristol
Health Sciences (BSc)

14:15 **Fiona Holmes**, University of Bristol
Health Sciences Research (MRes)

14:20 **Kate Ellacott**, University of Exeter
Intercalation Options at Exeter

14:30 **Anne Pullen**, University of Bristol
Cellular and Molecular Medicine Programmes

14:40 **Julie Browne**, University of Cardiff
Intercalation Options at Cardiff

14:50 **Matthew Ellis**, University of Bristol
Global Health (BSc)

14:55 **Richard Huxtable**, University of Bristol
Bioethics (BSc)

15:00 **Christian Gray**, University of Plymouth
Intercalate with Plymouth University

15:10 **Ailsa Cameron & William Turner**, University of Bristol
Childhood Studies (BSc)

15:15 **Patricia Denning-Kendall**, University of Bristol
Transfusion and Transplantation Science (MSc)

15:20 **John Lee**, University of Bristol
Medical Humanities (BA)

Detailed Schedule

15:30 Coffee and Tea Break

16:00 - 17:00

Workshop **(Theatre 1)**

My Career and the Impact of Intercalation

16:00 Talk 1: Dr Nick Bullock,
MBChB Cardiff, BSc Imperial, AFP Bristol, Surgical Core training.

16:15 Talk 2: Dr Olivia Jagger,
MBChB Bristol, BSc Bristol, AFP, National Medical Directors fellow

16:30 Talk 3: Dr Gabriel Galea,
BVetMed Lond, BSc Lond, PhD, Wellcome postdoc training fellow.

16:45 Talk 4: Dr Simon Thornton,
MBChB Bristol, BSc Bristol, AFP, Surgical Core trainee, GP lecturer

17:00 Meeting Close and Prize Awards **(Theatre 1)**
Professor Jonathan Sandy, Dean of Faculty of Health Sciences

17:15 **Wine tasting reception**
"UK vs France: an exercise in spotting local talent"

Nibbles and Networking

18:30 Depart

Abstracts for Oral Presentations

Theme 1: Cancer, Immunology and Infection

1 Bethany Kingston, Year 5, Oxford University

The Role of the Transcription Factor ZBTB1 in Lymphocyte Development

Lymphocytes have important roles in defence against infections, cancer biology and autoimmune disease. Understanding lymphocyte development is therefore essential in discerning these processes and in identifying new therapeutic targets for their treatment. Transcription factors, such as the recently characterised zinc finger and BTB (Broad complex. Tramtrack and Bric a brac) domain protein 1 (ZBTB1) have key roles in controlling lymphocyte development.(1) ZBTB1 has been shown to cause early impairments in lymphopoiesis. Germline Zbtb1 knockout mice demonstrate a profound T-cell deficiency from the early thymic precursor stage, with decreased immunoglobulin class switching and impaired response to T-cell dependent antigens.(2-3) However, whether ZBTB1 is important at subsequent stages of T-cell development or in mature T-cells has not been investigated. Here we use conditional knockout mice to show that ZBTB1 is critical at later stages of lymphopoiesis and in stimulated T-cells. Using a T-cell specific Zbtb1 knockout we demonstrate that ZBTB1 is required for T-cell development from the double positive stage onwards, with a reduction in double positive and single positive thymocytes, but not in T-cells that differentiate before this point. With a second model, in which Zbtb1 is deleted after the addition of 4-hydroxy tamoxifen, we show that ZBTB1 is also necessary for lymphocyte survival in response to in vitro stimulation. These results reveal new roles for ZBTB1 during T-cell development and activation, providing further evidence of its importance in lymphopoiesis and enabling the future identification of its transcriptional targets and downstream regulatory pathways.

References: Siggs, O. M. & Beutler, B. The BTB-ZF transcription factors. Cell Cycle 11, 3358–69 (2012). Siggs, O. M., Li, X., Xia, Y. & Beutler, B. ZBTB1 is a determinant of lymphoid development. J. Exp. Med. 209, 19–27 (2012). Punwani, D. et al. Transcription factor zinc finger and BTB domain 1 is essential for lymphocyte development. J. Immunol. 189, 1253–64 (2012).

Authors: Bethany Kingston, Consuelo Anzilotti, Owen Siggs, Richard Cornall

Theme 1: Cancer, Immunology and Infection

2 James Sun, Year 4, Cambridge University

A novel inhibitor of necroptosis in human breast and mouse mammary cell cultures.

Programmed cell death (PCD) facilitates the elimination of unwanted cells, thus having important roles in homeostasis and the normal development of eukaryotic organisms. Apoptosis is the best studied form of PCD, mediated by proteolytic caspases. However, recently a growing number of distinct forms of PCD have emerged. Necroptosis is a form of programmed necrosis which results in the release of immunogenic molecules dependent on receptor-interacting protein kinases 1 and 3. It has been implicated in injury following solid organ transplantation, inflammation and ischaemia. Necroptosis is triggered in response to a complex signalling cascade and therefore may offer potential for intervention at many levels of the molecular pathway.

Necroptosis can be induced in vitro following TNF stimulation under conditions of caspase inhibition, which releases the negative regulation of necrosome formation by caspase 8. This study aims to characterise cell death in response to TNF in normal and cancerous mouse mammary and human breast cell lines and determine the efficacy of a novel inhibitor of necroptosis.

Quantification of Annexin V staining by flow cytometry was used as a marker of cell death and it is shown that mouse mammary (4T1) and human breast cancer cells (MBA-MD-468) have the capacity to undergo apoptosis, or in conditions of caspase inhibition, a caspase independent form of cell death believed to be necroptosis. These results were confirmed by microscopic examination of cell cultures. Immunoblots and assays of executioner caspase activity verify cell death observed in this condition is caspase-independent. Further characterisation of the cell death observed in these cells was conducted by subjecting cultures to pre-treatment with different combinations of known inhibitors of apoptosis and necroptosis. Strikingly, the inhibitor CB2 which was originally developed as a pan-caspase (apoptosis) inhibitor is able to rescue the cells from both apoptosis and necroptosis hence suggesting potential for therapeutic use.

Here we show for the first time that mouse mammary and human breast carcinoma cells are able to undergo necroptosis in vitro in conditions where apoptosis is blocked. There is therefore potential that this type of cell death could be exploited in the molecular targeted treatment of cancer.

Authors: James J. Sun, Maximilian Blanck, Christine J. Watson

Theme 1: Cancer, Immunology and Infection

3 Natasha Daoud, Year 3, University of Bristol

The Role of Platelets and TGF-B in Prostate Epithelial and Cancer Cell Migration

Platelets play an essential role in cancer progression and metastasis. Tumour cell induced platelet aggregation facilitates immune evasion and the arrest of metastasising cells at distant sites in the microvascular circulation.[1] Platelets also release various cytokines and growth factors including ADP which aids cancer cell extravasation[2] and TGF-ß which promotes immunosuppression[3] and epithelial to mesenchymal transition.4 The aim of this study was to investigate the effect of platelets on the migration of normal prostate epithelial cells and prostate cancer cells and to describe the underlying mechanisms of action.

Migration assays revealed that platelet treatment of both normal epithelial PNT2-C2 cells and malignant PC3 cells increased cell migration significantly when compared to untreated controls. TGF-ß treated PNT2-C2 cells also displayed a significant increase in cell migration, suggesting that TGF-ß may be involved in the platelet mediated increase in cell migration. TGF-ß, and platelet-treated cells expressed pSmad-3, unlike controls, which indicates that TGF-ß may signal through a Smad-dependent pathway to elicit its effects on cell migration. TGF-ß-treated malignant DU145 cells did not demonstrate a significant difference in axial ratio, a measure of EMT, compared to untreated controls, however, this may have been due to the small sample size of cells measured.

Although these experiments need to be repeated, the results seem to suggest that TGF-ß released by platelets may regulate the platelet-mediated increase in cell migration. In order to prove this, cell migration assays need to be carried out with platelet-treated cells and a TGF-ß inhibitor. The cell migration assay can also be modified to determine the role of platelets and TGF-ß in invasion and extravasation.

References: S. Zheng, J. Shen et al. (2009) Platelets and Platelets and fibrinogen facilitate facilitate each other in protecting tumor cells from natural killer cytotoxicity. Cancer Sci. 100(5):859-65. D.Schumacher, et al. (2013) Platelet-Derived Nucleotides Promote Tumor Cell Transendothelial Migration and Metastasis via P2Y2 Receptor. Cancer Cell. 24(1):130-7. L.M. Wakefield & A.B. Roberts (2002) TGF-?? signaling:positive and negative effects on tumorigenesis. Current Opinion in Genetics and Development. 12(1):22–29. J. Xu, S. Lamouille & R, Derynck (2009) TGF-??-induced epithelial to mesenchymal transition. Cell Research. 19(2):156– 172.

Theme 1: Cancer, Immunology and Infection

4 Nathan Jenko, Year 6, University of Oxford

The correlation between T-cell receptor ligand affinity and T-cell activation at supraphysiologic affinities

Introduction: Harnessing the potential specificity and sensitivity of cytotoxic T-cells is a promising approach to improving the treatments available for cancer. This could either be done by modifying (transducing) autologous cytotoxic (CD8+) T-cells or by designing novel molecules, which interact with cancer antigens and T-cells (1). However, a prerequisite for such treatments is a thorough understanding of the T-cell receptor (TCR) and peptide-major histocompatibility complex (pMHC) kinetics. Specifically, one needs to identify the affinity of the TCR, which leads to the maximum activation of the cytotoxic T-cell.

Methods: In this study a panel of recombinant pMHCs was produced and their affinities for a specifically engineered recombinant high-affinity TCR were measured using surface plasmon resonance. A number of pMHCs with a wide range of affinities was then chosen. The ability of these pMHCs to activate T-cells was then assessed using a cellular model, specifically Jurkat cells transduced with the high-affinity TCR and an NFAT reporter gene.

Results: The results show that medium affinity TCR-pMHC interaction produces the maximum T-cell activation.

Discussion: Two apparent conclusions can be drawn from the data. Firstly, increasing the affinity of a TCR ligand beyond a certain point does not result in greater T-cell stimulation. This is in accordance with the predictions of the productive hit-rate model and is explained by the hypothesis that peptides can serially bind to TCR receptors after dissociating. The higher affinity reduces consecutive serial binding and hence T-cell activation (2). Secondly, since the highest activation was achieved by the pMHC with the medium affinity (Kd ˜ 10-10 M), while the pMHC with the lowest affinity (Kd ˜ 10-8 M) elicited less activation, the data suggests that the pMHC able to elicit the strongest T-cell activation has its dissociation constant around the nanomolar range.

References: N.J. Hassan and J. Oates. 'The T Cell Promise' EBR European Biopharmaceutical Review, no. SUMMER (2013): 72–74. S. Valitutti, S. Muller, M. Cella, E. Padovan, & A. Lanzavecchia. Serial triggering of many T-cell receptors by a few peptide MHC complexes. Nature 375, 148-151 (1995).

Theme 1: Cancer, Immunology and Infection

5 Amy Hodgkiss, Year 3, University of Bristol

The effect of Lrg1 on vascular integrity in uveitis

Uveitis is a sight-threatening condition caused by the trafficking of autoreactive T lymphocytes across a deregulated blood retinal barrier (BRB). Some factors involved in the regulation of BRB breakdown have been previously identified, however our understanding of the process remains incomplete. Leucine-rich alpha-2-glycoprotein 1(Lrg1) has recently been implicated in the angiogenic transforming growth factor ß 1 (TGFß1) signalling pathway through studies of the retinal vasculature.

In order to investigate the effect of Lrg1 on ocular vascular integrity during inflammation experimental autoimmune uveoretinitis (EAU) was induced in wildtype and Lrg1 knockout mice. Fluorescein angiography of these animals reveals that vascular integrity is most compromised during the acute inflammatory stage of EAU, and Lrg1 depletion reduces this early vascular leakage. Terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) of the retinae from these animals demonstrates that the absence of Lrg1 has no effect on the low levels of apoptosis in this tissue during EAU. However, zonula occludens 1 (Z0-1) immunohistochemistry of choroid flatmounts shows significant destruction of tight junction protein complexes as a result of EAU in wildtype mice. Lrg1 knockout mice appear protected from this destruction, indicating that it is mediated by a Lrg1-dependant mechanism.

Collectively the results from this study suggest a novel regulatory role for Lrg1 in the response of endothelial cells to inflammation. One plausible explanation for the data presented here is that Lrg1 diverts anti-inflammatory TGFß1 signalling by altering the stereochemistry of the TGFß1 receptor complex, changing its affinity for downstream signalling components.

Theme 1: Cancer, Immunology and Infection

6 Ikhuemose Ikhena, year 4, University of Oxford

Functional Characterisation of a Regulatory Variant Associated with Rheumatoid Arthritis in the MHC Class II

Rheumatoid arthritis is a multifactorial disease with the major genetic risk association involving the Major Histocompatibility Complex (MHC), specifically variants in the region of HLA-DRB1. The shared epitope hypothesis attempts to explain this risk by recognising that the strongly associated rheumatoid arthritis haplotypes, such as HLA-DRB*0101 and HLA-DRB*0401, share a highly similar amino acid sequence. However, different haplotypes that possess the shared epitope have greatly differing rheumatoid arthritis risk. Decreased expression of HLA-DRB1 could provide an explanation for the increased risk of rheumatoid arthritis of some shared epitope haplotypes by increasing the chance for autoreactive T cells to escape negative selection in the thymus.

Here we characterise the rheumatoid arthritis-associated variant, rs9271574, located in the intergenic element XL9 between HLA-DQA1 and HLA-DRB1, and show that the variant could be responsible for haplotype-specific gene expression of HLA-DRB1 via a luciferase reporter gene assay. The HLA-DRB1 promoter results indicate DRB*0401 (rs9271574=T) monocytes exhibit lower expression of HLA-DRB1 than DRB*0101 (rs9271574=G) monocytes; and site-directed mutagenesis of XL9DRB*0101 from T to G at rs9271574 had a similar effect on gene expression. This finding was supported by evidence of allele-specific transcription factor binding to rs9271574 in a chemiluminescent electrophoretic mobility shift assay (EMSA), in which the G allele displayed preferential transcription factor binding. Bioinformatic analysis using transcription factor binding prediction software revealed the transcription factors SOX10 or XBP-1 could be responsible for the transcription factor allele-specific binding observed in the EMSA.

Our data highlights the role of genetic variation in the region of XL9 regulating MHC class II gene expression, specifically rs9271574 and HLA-DRB1 transcription and provides a genetic explanation for the variation in risk of anti-CCP positive rheumatoid arthritis across shared epitope HLA-DRB1 haplotypes.

Theme 2: Cardiorespiratory, Endocrine and Neuroscience

7 Samuel Simpson, Year 5, Sheffield University

Expression analysis and knockdown of the novel MS-causing gene GRAMD1B during zebrafish development.

Introduction: Multiple sclerosis (MS) is an inflammatory autoimmune disorder of the central nervous system with largely unknown aetiology and no known cure.

Collaborative clinicians in Milan identified a consanguineous family with hereditary MS arising from a single nucleotide polymorphism in the gene GRAMD1B. GRAMD1B is expressed in immune cells, and is highly conserved across species.

Aims: Investigate GRAMD1B expression in the zebrafish by in situ hybridisation.

Perform transient overexpression and morpholino knockdown of GRAMD1B in wild-type zebrafish embryos, to characterise the effect of gene function on zebrafish development and immune cell physiology in vivo.

Methods: Sense and antisense GRAMD1B RNA probes were produced to determine special expression of GRAMD1B in the zebrafish embryo.

Doses of 25 to 200pg GRAMD1B mRNA, or 1 to 8ng GRAMD1B morpholino were injected into 1-cell wild-type and transgenic zebrafish embryo siblings with appropriate controls, and development assayed up to 72 hours post fertilisation (hpf).

Results: In situ hybridisation revealed GRAMD1B mRNA expression in the zebrafish hindbrain and neuromasts at 48hpf.

Overexpression of GRAMD1B mRNA does not produce a overt developmental phenotype in the zebrafish.

Knockdown of GRAMD1B in wild-type zebrafish larvae produces a distinct developmental phenotype and reduces the number of microglia within the zebrafish optic tectum at 72hpf.

Discussion: These in vivo experiments of GRAMD1B function support a role in zebrafish brain development, providing avenues of further research to better understand the aetiology and disease process of MS.

Author: S.J. Simpson, E. Stupka, F. M.Boneschi, D. Lazarevic, A.M. Osiceanu, S.A. Renshaw.

Theme 2: Cardiorespiratory, Endocrine and Neuroscience

8 Natalie Lewis, Year 4, Cardiff University

Investigating whether the invasive respiratory pathogen Aspergillus fumigatus can evade innate immune recognition

Introduction: Aspergillus fumigatus (A. fum) is an airborne fungus, which can be an invasive respiratory pathogen in immunosuppressed individuals or those with lung disease. A. fum's virulence factors include the secretion of proteases. I hypothesise that these proteases are capable of cleaving the fungal innate immune receptor dectin-1 to aid A. fum's evasion of innate immune recognition. In addition to this I hypothesize that neutrophil elastase is also able to cleave dectin-1. There are two functional isoforms of dectin-1 in humans: Isoform A and isoform B. My aim was to test whether these isoforms are differentially susceptible to cleavage by proteases.

Methods: NIH-3T3 fibroblasts transduced to express human dectin-1 isoform A or isoform B with a haemagglutinin tag were used. Cells were incubated for 45 minutes at 37°C with neutrophil elastase or the supernatants of two strains of A. fum: CEA10 which has active proteases or Af293 which has 0 units of protease activity. PMSF and alpha-1 antitrypsin were used as protease inhibitors. Dectin-1 expression was analysed by fluorescence-activated cell sorting. Western blot was used to look for evidence of proteolytic cleavage. 4 concentrations each of neutrophil elastase, CEA10 and Af293 supernatants were incubated with soluble human dectin-1 for 60 minutes in a water bath at 37°C.

Results: Neutrophil elastase and CEA10 proteases decreased expression of dectin-1 isoform A when compared to expression on cells in buffer. PMSF and alpha-1 antitrypsin were both found to have protective effects. Western blot showed bands for protein fragments at a lower size, demonstrating that neutrophil elastase and CEA10 proteases cleave dectin-1. Dectin-1 isoform B was not susceptible to cleavage.

Discussion: The CEA10 strain of A. fum proteolytically cleaves dectin-1 isoform A off the membrane of cells, highlighting a previously unrecognised mechanism, which may enable A. fum to evade innate immune recognition. Neutrophil elastase also proteolytically cleaves dectin-1 isoform A, a factor that might increase the susceptibility of cystic fibrosis patients to infection with A. fum. Individuals that preferentially express isoform B might have an advantage for protection against A. fum. These novel findings might aid the development of therapeutic approaches in the future.

Authors: Natalie Lewis (Cardiff University), Sarah Herrick (University of Manchester), Janet Willment (University of Aberdeen), Gordon D. Brown (University of Aberdeen), Eamon McGreal (Cardiff University)

Theme 2: Cardiorespiratory, Endocrine and Neuroscience

9 Anuriti Aojula, Year 3, University of Birmingham

Decorin reduces communicating hydrocephalic pathology: a diffusion tensor imaging and immunohistochemical study.

Juvenile communicating hydrocephalus is characterised by transforming growth factor-beta (TGF-ß) mediated fibrosis of the arachnoid granulations, resulting in cerebrospinal fluid accumulation and subsequent ventricular system enlargement. Although the TGF-ß antagonist, Decorin, prevents ventricular dilation(1), its ability to inhibit ventriculomegaly induced cerebral damage is yet to be assessed. Furthermore, the capacity for diffusion tensor imaging (DTI) to act as a proxy measure of hydrocephalic pathology has not been examined. Hence, this study aimed to decipher whether DTI parameter abnormalities correlate with pathology in communicating hydrocephalus and if Decorin prevents such aberrations. Therefore, communicating hydrocephalus was produced by injecting kaolin, a fibrosis-inducing agent, into the basal cisterns of the subarachnoid space in all but four three-week old rats (n=19). Immediately post kaolin injection, phosphate buffered saline (n=6) or Decorin (n=5) was delivered continuously for two weeks intraventricularly, before rats were DTI scanned and sacrificed. The DTI mean diffusivity, fractional anisotropy, radial and axial diffusivity of seven cerebral regions was assessed by voxel-based analysis. Using immunohistochemistry, myelin (MBP) integrity, astrocyte (GFAP), microglial (OX-42), lipid peroxidation (4-HNE) and aquaporin-4 (AQP4) levels, the latter indicative of hydrocephalic oedema when raised were examined in eight caudal cerebral structures. Our DTI findings have revealed that communicating hydrocephalic pathology is predominantly located in the caudal cerebrum. Moreover, Decorin's therapeutic potential to decrease myelin damage in the caudal internal capsule and prevent caudal periventricular white matter (PVWM) oedema and astrogliosis has been highlighted by our study. Furthermore, as DTI parameter values predominantly correlated with PVWM astrocyte and aquaporin-4 levels, the clinical utility of DTI to act as a surrogate marker of PVWM but not global communicating hydrocephalic pathology has also been discovered.

Reference: Botfield H, et al. Decorin prevents the development of juvenile communicating hydrocephalus. Brain 136: 2842-2858, 2013. No conflicts of interest for any authors.

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Theme 2: Cardiorespiratory, Endocrine and Neuroscience

10 **Cian Wade**, Year 4, University of Oxford

Post-movement beta activity in sensorimotor cortex indexes confidence in estimations from internal models

Sensorimotor adaptation is crucial in maintaining accuracy of movements in a changing environment. Computational models of sensorimotor control show that the rate of movement error reduction is determined by the prediction error history in a manner predicted by Bayes' theorem. Additionally, previous studies have shown that post-movement event-related beta synchronisation (PMBS) amplitude in contralateral sensorimotor cortex (CSMC) is modulated by the size of visuomotor error. In the present study, we aimed to synthesise these two observations by investigating whether prediction error history modulates both the adaptive behaviour and the amplitude of the PMBS of subjects undertaking a visuomotor adaptation task in a manner consistent with Bayes' theorem.

EEG was recorded in 15 young, healthy subjects during a visuomotor joystick adaptation task. Prediction error history was manipulated by presenting two different experimental conditions in counter-balanced order to each subject. Conditions differed in the sequences of the angle of perturbation between the joystick's movement and the on-screen visual feedback.

We found that the rate of error reduction was greater after a period of no angular perturbation trials compared to random angular perturbation trials and that this was associated with a significant reduction in PMBS amplitude. Conversely, when prediction error history was similar across both conditions, the rate of adaptation and the decrease in relative PMBS amplitude were not significantly different. Hence our data suggest that both the PMBS amplitude and adaptive behaviour are modulated by prediction error history in a manner predicted by the Bayesian framework.

These findings argue that the PMBS is an index of the relative confidence placed in the current state of the internal model versus the current trial's prediction error, a weighting determined by Bayesian contextualization of the recent history of sensorimotor errors. As such, the PMBS is a good candidate for a neural correlate of the internal representation of uncertainty in sensorimotor control. This work sheds further light on the controversial function of beta oscillations in the sensorimotor system and may provide insight into how aberrancy of beta activity contributes to motor impairments in disease.

Authors: Cian Wade (University of Oxford), Huiling Tan (University of Oxford), Peter Brown (University of Oxford)

Theme 2: Cardiorespiratory, Endocrine and Neuroscience

11 Jonathan Chuo Min Lee, Intercalation Year, University of Bristol

The Role of Group II Metabotropic Glutamate Receptors in the Cornu Ammonis 2 Region of the Hippocampus

Introduction: Group II metabotropic glutamate receptors (mGluR) have been known to depress neuronal transmission via inhibition of neurotransmitter release at glutamatergic synapses. They can also mediate long term depression in several regions of the brain including the lateral amygdala and striatum. However, their roles in the hippocampus, particularly the cornu ammonis 2 (CA2) region is largely unclear.

Objectives: Our research aims to elucidate the physiological and pharmacological profiles of group II mGluRs within the CA2 and will study their significance in mediating plasticity within the CA2.

Methods: We have used electrophysiological techniques on wildtype and mGluR2 deficient rats in combination with group II mGluR modulating drugs.

Results and Discussion: Using DCG-IV (group II mGluR agonist), we have identified that activation of group II mGluRs leads to depression of synaptic transmission in the TAP-CA2 synapse in a dose-dependent manner. Washout of DCG-IV resulted in LTD which indicates that group II mGluRs can mediate LTD in the same region. Using LY541850 (mGluR2 agonist, mGluR3 antagonist) on wildtype rats, DCG-IV on mGluR2 deficient rats, we have further evidence that activation of mGluR 2/3 alone can induce significant depression of synaptic response as well as induce LTD. We also found that activation of either subtype of group II mGluRs does not saturate the slice to further depression during activation of the other group II mGluR subtype. We thus established that mGluR2 and mGluR3 may have synergistic effects on one another, potentiating depression and lowering the threshold for LTD induction. Finally, we found that the chemical LTD obtained during drug application does not saturate the synapse to subsequent electrical LTD stimulated using a low frequency stimulus (1Hz, 900 stims), the converse is also true. This shows that both processes may not be mechanistically equivalent.

Conclusion: These results suggest important roles of group II mGluRs as regulators of CA2 activity which may have significant implications in explaining the mechanism behind the clinically beneficial (eg. neuroprotective/anxiolytic) effects of group II mGluR modulation. These results will also help tease apart the physiological role of the CA2 in the construction of episodic memory in the hippocampus.

Authors: Jonathan Lee Chuo Min, Joshua Latham and Dr Zuner Bortolotto

Theme 2: Cardiorespiratory, Endocrine and Neuroscience

12 Joe Finney, Year 4, Cardiff University

Studying the re-innervation of dopaminergic neurons in a zebrafish model

Introduction: Regenerative therapies may represent a major step forward in the treatment of Parkinson's Disease, but more must first be learned about the mechanisms of regeneration. The zebrafish is an excellent model for these studies, owing to its spectacular powers of neuroregeneration.

Previous work has found that zebrafish dopaminergic neurons are regenerated following ablation by the toxin 6-hydroxydopamine-but it was not known whether or not the newly-produced neurons successfully re-innervated their targets. This project set out to answer this question, and also to determine what effect immune stimulation, known to play a role in initiating regenerative responses, might have on the process.

Methods: A digital image analysis technique was developed to quantify the innervation of the target field of a toxin-sensitive population of dopaminergic neurons by tyrosine hydroxylase immunostained axons. This technique was applied to brain sections taken from an experiment in which zebrafish were treated with the toxin and harvested at multiple time-points over the following 18 months. Statistical comparisons were made between time-points and with a control group to determine how innervation of the field changed over time.

A similar method was used to determine the effect of injecting Zymosan A, an immunogen, following toxin treatment.

Results: It was found that the innervation of the population under study did not recover to control levels within 18 months, and that no significant change in innervation occurred between 2 and 540 days. It was also found that immune stimulation by Zymosan A did not have a significant effect on re-innervation within the study period.

Discussion: The finding that regenerating zebrafish dopaminergic neurons do not re-innervate their target field was unexpected given that other cell types in the zebrafish central nervous system are known to do so successfully. The reasons for this disparity are unknown, perhaps a detrimental environmental change occurs after ablation, or important pathfinding signals may be missing. Further work could study different populations and different methods of destroying the neurons, for example genetic ablation, to see whether these have any influence on the results.

Authors: Joe Finney, Nick Davies, Professor Catherina Becker, Professor Thomas Becker

Theme 3: Epidemiology, General Practice and Global Health

13 Georgina Prestwich, Year 4, University of Bristol

Menstrual hygiene management amongst schoolgirls in Uganda and the impact on their education: a cross sectional study

Introduction: An increasing number of studies have found that girls in low-income settings miss or struggle at school during menstruation if they are unable to manage their menstrual hygiene effectively. This study explores the menstrual hygiene practices and knowledge of girls at rural government primary schools in the Rukungiri district in Uganda and assesses the extent to which poor menstrual hygiene management (MHM) affects their education.

Methods: A self-administered questionnaire was completed by schoolgirls in six government-run primary schools in the Rukungiri district. Focus groups were held with girls from each school and semi-structured interviews were conducted with headteachers and female teachers from the participating schools. A toilet assessment was also conducted in each school.

Results: One hundred and forty schoolgirls completed the questionnaire. The girls reported a lack of access to adequate resources, facilities and accurate information to manage their menstrual hygiene effectively at school. They reported that, as a result, during menstruation they often struggle at school or miss school. Eighty-six girls (61.7%) reported missing school each month for menstrual-related reasons (mean 1.64, range 0-10, SD. 1.84).

Conclusion: It is common for girls who attend government-run primary schools in the Rukungiri district to miss school or struggle in lessons during menstruation because they do not have access to the resources, facilities, or information they need to manage for effective MHM. This is likely to have detrimental effects on their education and future prospects. A large-scale study is needed to explore the extent of this issue.

References: Robyn Boosey, Georgina Prestwich, Toity Deave. Menstrual hygiene management amongst schoolgirls in the Rukungiri district of Uganda and the impact on their education: a cross-sectional study. The Pan African Medical Journal. 2014;19:253

Authors: Georgina Prestwich, Robyn Boosey, Toity Deave

Theme 3: Epidemiology, General Practice and Global Health

14 Rob Ayres, Final Year, University of Southampton

Omega-3 long chain polyunsaturated fatty acids in human health: a link between obesity and status?

Omega-3 long chain polyunsaturated fatty acids (n-3 LCPUFAs) are beneficial for human health but despite this, UK status remains low. Although mainly attributable to poor fish consumption, the recent discovery and development of the red blood cell (RBC) membrane and abdominal adipose tissue (AT) as accurate and reliable markers of long term status means diet-independent factors affecting status can be elucidated. This study explored body mass index (BMI) as one such factor, investigating its impact on RBC and abdominal AT status in 100 healthy volunteers. This was achieved through a randomised control trial, collecting blood and abdominal AT samples before and after a 12 week fish oil or placebo supplementation period. Fatty acid methyl esters were synthesised from each sample and gas chromatography was used to determine their fatty acid composition. Comparisons in baseline status, incorporation changes and biomarker interaction were made between lean and obese BMI groups, along with age and sex, two known non-dietary status factors. At baseline, RBC and AT eicosapentaenoic acid and docosahexaenoic acid (EPA+DHA) levels positively correlated ($p<0.001$). Between BMI groups, no differences were present in RBC or AT n-3 LCPUFA levels, although obese subjects had higher AT docosapentaenoic acid ($p<0.05$) levels. RBC and AT EPA+DHA levels increased with age, a trend only present in the lean cohort ($p<0.05$). Conversely, AT arachidonic acid levels only increased with age in obese subjects ($p<0.05$). Following fish oil supplementation, RBC EPA levels increased more in lean compared with obese individuals ($p<0.01$), while RBC DHA levels increased at the same rate in both BMI groups. Although no differences in AT n-3 LCPUFA incorporation rate between BMI groups were present, AT DHA levels increased more in lean compared with obese males ($p<0.05$). BMI had no impact on n-3 LCPUFA biomarker distribution. Although not yet warranting a change to dietary advice or supplementation dosing for different BMI groups, obesity did alter n-3 LCPUFA status and response to supplementation. Additional investigations using varying fish oil concentrations and different AT depots over a longer time period should be undertaken to further understand BMI as a non-dietary factor influencing n-3 LCPUFA status.

Authors: Ayres RB West AL Fisk HL Paras-Chavez C Calder PC

15 **Elizabeth McGeorge**, Year 4, University of Birmingham

Incidence and spectrum of health problems and health service utilisation among backpackers in Thailand

Introduction: Previous research suggests backpackers are at increased risk of health problems compared to other groups of travellers.[1] Southeast Asia is the region most popular with backpackers-[2] with Thailand the most visited country.[3] This study aimed to determine the incidence and spectrum of health problems and quantify health service use among backpackers visiting Thailand.

Methods: A cross sectional survey was distributed to English speaking backpackers aged 18 years or over, recruited by convenience sampling in ferry terminals on the islands of Koh Pha-Ngan and Koh Tao, Thailand.

Results: Of the 1680 questionnaires analysed, 79.8%(n=1340) reported a health problem, most commonly: insect bites (60.4%-n=1015/1680), sunburn (47.7%-n=802/1680) and diarrhoea (43.6%-n=733/1680). Backpackers taking part in a 'risky activity' (land/water sports or vehicle rental) were 3 times more likely to report a health problem (OR 3.3-95% CI 2.2–4.8-p<0.001) and 7 times more likely to report an accident (OR 7.3-95% CI 2.3–23.2-p<0.001). 14.8%(n=249) participants reported involvement in an accident, the majority of which were vehicular (n=149) with over half (58.2%-n=145) reporting injuries as a result of their accident 23.2%(n=387) participants visited health service/s during their trip, three quarters of which (76.7%-n=279) visited a pharmacy.

Discussion: The study identified a higher incidence of health problems and health service utilisation than previously reported among travellers visiting Thailand.[4-5]. Further research is needed to establish the adequacy of pre-travel health advice among the backpacking population, however as the majority of reported problems were easily preventable, advice regarding personal precautions to reduce the risk of common health problems should be reinforced prior to travel. Backpackers commonly reported engaging in 'risky activities' whilst abroad. Given the increased risk of health problems following participation in such activities, pre-travel advice promoting awareness of the implications of risky behaviour, in addition to general road safety advice, should be promoted to backpackers.

Authors: Elizabeth McGeorge, Dr Gilles de Wildt, Dr Sabrina Grant

Theme 3: Epidemiology, General Practice and Global Health

16 Georgina Frew, Year 4, University of Birmingham

Hepatitis B: knowledge, attitudes and practices amongst backpackers in Thailand

Objectives: Hepatitis B can cause acute illness and long-term complications. In 2013, 200, million tourists visited countries that are endemic for hepatitis B virus (HBV). Backpackers are potentially at greater risk of hepatitis B than other travellers, yet, exposure to HBV remains under researched in this population. Thailand is a popular backpacker destination with endemic HBV. This study aimed to determine the proportion of backpackers in Thailand who are at high risk of HBV exposure and identify the factors associated with exposure and immunisation.

Methods: A cross-sectional survey of backpackers visiting two islands in Thailand was performed during February and March 2015. Participation in activities with high HBV exposure risk was recorded, alongside rates of vaccination and an evaluation of knowledge and attitudes towards the risk of HBV.

Results: 1680 questionnaires were completed and analysed; the median participant age was, 24 (range: 18-68) and 47.9% were male. 80% of participants reported seeking pre-travel health advice. 332 (20.8%) took part in activities with a high risk of HBV exposure; exposure was associated with younger age, male gender and longer trip duration. Over two-thirds of the sample reported no protection against HBV. 370 (24%) were able to correctly identify HBV transmission methods and 740 (44.1%) were unaware of the risk of HBV in Thailand or considered it to be low.

Conclusion: The proportion of backpackers in Thailand participating in high-risk activities was double the level found in previous studies that have examined the HBV exposure risk amongst travellers to endemic countries. Voluntary risk activities were the largest source of potential exposure to HBV and rates of vaccination are low. Backpackers should consider vaccination against HBV and the pre-travel health consultation should include education on risk behaviours, particularly sexual health and body modification.

Authors: Georgina H Frew, Dr Gilles de Wildt, Dr Sabrina Grant

Theme 3: Epidemiology, General Practice and Global Health

17 Sarah Johnson, Year 4, Cardiff University

Model to investigate the relative effects of auditory and visual distractions in an operating theatre environment

Introduction: Auditory and visual distractions have been shown to have a negative effect on individuals' ability to carry out manual and cognitive tasks1, 2. However, there is little research on its effects in a surgical setting. The Royal College of Surgeons Edinburgh recommend a 'sterile cockpit' environment during some points of surgery. This preliminary study aims to evaluate the effects of auditory and visual distractions on individuals' ability to carry out a simple task of manual dexterity using a simulated laparoscopic model.

Methods: 72 participants were recruited to carry out a task involving placing pins into a Purdue pegboard via a live video feed. Participants carried out four trials, each of which lasted 90 seconds: i) static video feed and silence; ii) static feed and background noise; iii) rotating feed and silence; iv) rotating feed and background noise. Participants were randomly allocated to ignore, monitor or respond to target tones by reading a number from a second screen.

Results: Noise did not significantly affect an individual's pin score, regardless of whether they are required to ignore, monitor or respond to the noise. Screen rotation (which often happens in laparoscopic surgery) caused a statistically significant decline in participants' pin score but did not significantly interact with any other factors.

Discussion: Our findings show that in a simple repetitive task there was no detriment to fine motor skills when noise was introduced. This may be because the task was not as manually or cognitively demanding as laparoscopic surgery, so individuals were still able to process distracting stimuli without interrupting the primary task. Screen rotation did have significant effects on pin score, but not when combined with other distracting factors. This correlates with previous research in surgical and non-surgical settings2. Further work is required in a more complex simulated situation.

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Authors: SJ. Johnson, R. McLeod, W. Macken.

Theme 3: Epidemiology, General Practice and Global Health

18 Niall McCartan, Year 5, University of Liverpool

The impact of an educational intervention on patient assessment and communication skills in escalation of care.

Objective: This study aimed to determine whether an educational intervention could improve the performances of junior doctors in escalating the care of an acutely deteriorating postoperative patient.

Introduction: Surgical complication rates remain consistent yet mortality rates vary. This variation in mortality, called failure to rescue, indicates that the quality of postoperative care is a major determinant of surgical outcomes. Escalation of care, the recognition, communication and response to patient deterioration, is integral to postoperative care, yet junior doctors receive little formal training on the process.

Methods: Junior doctors were recruited to complete two simulated scenarios requiring escalation of care. They were randomised to an intervention group, who received teaching before completing their second scenario, or a control group who received the teaching after completing both scenarios. Scenarios were video-recorded and retrospectively rated using 3 validated assessment scales. The Surgical Ward-care Assessment Tool measured patient assessment and management skills, the Quality of Information Transfer tool assessed communication skills, and the W-NOTECHS scale assessed nontechnical skills. The scores achieved in both groups were compared. All participants completed pre, and post-study questionnaires and gave feedback.

Results: Thirty-three participants were randomised to intervention (n=18) or control (n=15) groups. Baseline demographics were well matched between both groups. There were no score differences between the groups at baseline. In the second scenario, the intervention group demonstrated significantly better patient assessment (median 9.5 vs. 7, $P<0.001$), communication (90 vs. 75, $P<0.001$), and nontechnical (16 vs 13, $P<0.001$) skills.

Discussion: Introducing a systematic approach to escalation of care led to improved patient assessment, information transfer and nontechnical skills in junior doctors, and could improve patient outcomes if implemented effectively. Earlier recognition and response to patient deterioration can improve the quality of postoperative care and may reduce failure to rescue rates.

Authors: Niall McCartan
Supervisors: Max Johnston and Sonal Arora

Abstracts for Poster Presentations

Theme 1: Cancer, Immunology and Infection

19 Rui-En Chung, Year 5, University of Southampton

Induction of oxidative stress as a therapeutic strategy in MLH1 deficient disease.

Introduction: MLH1 a key protein in DNA mismatch repair pathway is known to be deficient in various tumour types as MLH1 loss leads to increased susceptibility to gene mutations that contribute to carcinogenesis. Significantly no therapies currently exist specifically targeting MLH1 deficient cancers. MLH1 deficient colorectal cancer were found to be less sensitive to certain chemotherapy such as 5-flurouracil. Utilising the principle of synthetic lethality MLH1 deficient cells were found to be sensitive to oxidative DNA damage upon silencing of mitochondrial genes. Subsequent work elucidated a potential role for MLH1 in the repair of both nuclear and mitochondrial DNA and that MLH1 deficiency may lead to mitochondrial dysfunction which could be directly related to the findings of its vulnerability to mitochondrial targeted agents. The project's objectives are to validate the selectivity of mitochondrial targeted agents to MLH1 deficient cell lines by using Parthenolide a reactive oxidative species(ROS) inducing agent and to determine the role of the anti-oxidative response pathway in MLH1 deficient cells

Methods: The HCT116 and HCT116+chr3 cell lines were used to represent MLH1 deficient and MLH1 proficient cells respectively. Both cell lines were drugged with Parthenolide for 5 days and cell viability was analysed using a luciferase-based ATP assay. Cell viability was also analysed upon Parthenolide treatment in the presence of N-acetyl cysteine or Apocynin. Protein expression of NRF-2 and Keap-1 was determined by Western blot analysis. All experiments were repeated three times.

Results: We validated that Parthenolide is selectively cytotoxic in MLH1 deficient cells by inducing ROS. NOX may play a role in the Parthenolide mechanism of action by producing superoxide. Increase Keap-1 expression and decrease NRF-2 expression suggests that the anti-oxidative response may play a role in the sensitivity of MLH1 deficient cells to oxidative-stress.

Discussion: This project has validated the selectivity of Parthenolide for MLH1-deficient cell lines by inducing lethality through ROS generation and oxidative stress and suggests a potential dysfunction in its anti-oxidative stress response.

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Authors: Rui En Chung Sukaina Rashid Sarah A Martin

Theme 1: Cancer, Immunology and Infection

20 Hannah Wilson, Year 6, Imperial College, London

'PATCH'-ing up toxicities of contemporary ADT for prostate cancer

Introduction: Prostate cancer remains both a large clinical and financial burden. With over 11,000 cases diagnosed each year in the UK and an NHS bill costing over £100 million, there is a need to seek better and more affordable treatments for this complex disease. Hormonal therapies, namely androgen deprivation therapy, are currently used as effective management. However the side effects of such treatment, namely reduced bone mineral density (BMD) and osteoporosis increase the clinical burden created by prostate cancer. Therefore there is a need to better identify those patients at risk of developing such conditions and reducing fracture risk. Methods. The current approach to assessing fracture risk is Dual Energy X-ray absorptiometry (DEXA) scans and BMD. This only accounts for about 40–50% of the in vitro compressive strength of bone. Rather 'bone quality' is an amalgamation of factors including the micro-architecture, quality of collagen, the rate of bone turnover. As such we began looking at clinical CT scans (that the patients had had for cancer staging) that had been done at the same time as DEXA scans and assessing the information we could gather from these scans. Results. Preliminary results indicate that the CT scans could provide a more accurate indicator of overall bone quality by the ability to assess the bone volume fraction (BVF) and bone strength using fine element analysis (FEA). Conclusion. There is a pressing need to identify cancer patients who are at risk of fracture from cancer-related treatments. Prostate cancer patients undergoing Androgen deprivation therapy (ADT) exemplify this. The current gold standard for fracture risk using DEXA scan only reflects 50% of the picture. PATCH (Prostate Adenocarcinoma: TransCutaneous Hormones) patients represent an excellent patient group to assess bone strength over time with coordinated DEXA and CT scans.

Authors: Hannah Wilson R.Abel, I. Shah, P.Abel, P.Price, L.Honeyfield

Theme 1: Cancer, Immunology and Infection

21 Alexander Fahmy, Year 6, University of Birmingham

Efflux inhibitors as a novel strategy to prevent biofilm formation on internal medical devices

Introduction: Bacterial biofilms are frequently responsible for medical device associated infections that can result in serious clinical consequences. The unique properties of biofilms make them highly resistant to antibiotic agents and therefore refractory to conventional medical therapy. This makes novel, non-antibiotic, anti-biofilm strategies highly sought after. One such approach is through efflux inactivation. This study tested the efficacy of efflux inhibitors (EIs) against biofilms formed on clinically relevant medical biomaterials.

Methods: Crystal violet biofilm formation assays were used to assess the inhibitory effect of single or paired EIs against multiple nosocomial bacterial biofilms. A clinical model of an infected medical device was created by allowing biofilms to form on materials that constitute intravascular catheters, endotracheal tubes and orthopaedic prostheses.

Results: The investigated EIs, many of which are in use in clinical practice, were able to induce a significant reduction in biofilm formation on all the surfaces tested. EIs were more effective at preventing biofilm formation rather than removing biofilms preformed on medical devices. This effect was observed at a lower concentration when two agents were used together. However, the effects of EIs were strain and material specific and there was no universal biofilm inhibitor.

Conclusions: Chemical efflux inhibition is a promising approach to reduce biofilm formation on a variety of implant surfaces. To continue to develop this anti-biofilm strategy further work would need to identify EIs with a broader spectrum activity.

Theme 1: Cancer, Immunology and Infection

22 Emma Johnston, Year 4, Leeds University

The role of Met endosomal signalling in breast cancer cell migration

Unable to attend to present –

Theme 1: Cancer, Immunology and Infection

23 Bakir Al-Dulaimy, Barts and The London School of Medicine & Dentistry

Gene Expression Patterns in Oral Squamous Cell Carcinoma Cancer Stem Cell Phenotypes and their Significance

Background: The majority of cancer-related deaths are caused by tumour invasion and secondary metastases. This is particularly true for head and neck cancers due to the close proximity of the lymphatic system and vital organs. The developmental processes of epithelial-to-mesenchymal transition (EMT) and mesenchymal-to-epithelial transition (MET) are hijacked by tumours to drive tumour invasion and metastasis. There is strong evidence linking EMT/MET and cancer stem cells (CSCs) which initiate and maintain tumours. In oral squamous cell carcinoma (OSCC), a sub-population of CSCs that has undergone EMT has been identified and these cells have been shown to have migratory and mesenchymal characteristics.

Aims: This study aimed to investigate genes differentially expressed between non-EMT CSCs and EMT CSCs in OSCC. A further aim was to elucidate functional effects of down-regulation of genes that could be identified as differentially expressed.

Methods: Differentially expressed genes were initiallyidentified using mRNA microarrays prepared for the two CSC populations. Real time quantitative polymerase chain reaction (RT qPCR) was then used to validate expression levels of differentially expressed genes. Down-regulation of two genes identified was then achieved by small interfering RNA (siRNA)-mediated knockdown. Changes of cell characteristics were analysed by phase microscopy and flow cytometry.

Results: 40 separate genes were found to be differentially expressed between non-EMT CSCs and EMT CSCs. Consistent differences across several OSCC cell lines was used to narrow down the gene list to 16 targets. RT qPCR was used to confirm these genes which revealed OVOL1 and OVOL2 to be of particular interest due to their marked and statistically significant higher expression levels in non-EMT CSCs across three OSCC cell lines. Knock down of OVOL1 and OVOL2 lead to morphological changes consistent with mesenchymal characteristics. Flow cytometry confirmed a significant increase in the proportion of EMT CSCs after siRNA-mediated OVOL knockdown in cells across three OSCC cell lines.

Conclusion: Through the use of multiple mRNA microarray analysis from OSCC cell lines, we identified several genes that were differentially expressed between two distinct CSC phenotypes (non-EMT and EMT). These genes may serve as potential markers for prognosis. Further investigations of OVOL1 and OVOL2 genes suggest that they play essential roles in cancer biology, specifically within the cancer stem cell and EMT/MET paradigm. Further work may reveal OVOLs to be extremely useful targets in improving treatment, diagnosis and prognosis of OSCC.

Authors: Bakir Al-Dulaimy Professor Ian Mackenzie

Theme 1: Cancer, Immunology and Infection

24 Matthew Dickinson, Year 6, University of Bristol

Subcellular distributions of signalling intermediates during the activation of primary T cells.

T lymphocyte function is regulated by complex signalling networks. Following activation, T cell signalling intermediates show unique enrichment patterns within both time and space. Quantitative description of these spatiotemporal patterns allows for an analysis not only of each protein in its own right, but also in relation to other signalling intermediates in space and time. This builds a systems-scale analysis with the study of additional molecules. A map-like spatiotemporal overview may highlight elaborate signalling networks, and how these networks regulate a flow of information from the molecular level to actual cell function. The main protein of interest in this project was lymphocyte-activation gene 3 (LAG-3), an MHC II ligand with negative co-stimulatory activity in T cells.

Plasmid constructs containing the gene for LAG-3 with an enhanced green fluorescent protein (EGFP) tag were produced using bacterial transformations. A retroviral vector was used to transduce constructs into murine T cells, which were then activated ex vivo with antigen-presenting cells (APCs). Using live cell fluorescence microscopy, LAG-3 distributions were described quantitatively for future integration into an ongoing systems-scale analysis.

LAG-3 in murine transgenic T cells appeared to enrich transiently at the T cell:APC interface in T cells but this was not quite statistically significant (P=0.057), with a slight preference for a central accumulation pattern. LAG-3 was observed in large intracellular pools during T cell activation. Two further proteins; vasodilator-stimulated phosphoprotein (VASP) and protein kinase zeta (PKCζ) were cloned into plasmid constructs with EGFP sensors. These observations may provide a foundation towards understanding LAG-3 trafficking during T cell activation and insight into signalling networks involving LAG-3.

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Theme 1: Cancer, Immunology and Infection

25 Mohammed Chowdhury, Year 4, Cardiff University

Molluscum contagiosum Virus MC084 epitopes for use in a MCV ELISA, and MC084 cross-reactivity with Vaccinia virus H3L

Unable to attend to present

Theme 1: Cancer, Immunology and Infection

26 Andrew Jones, Year 4, University of Bristol

Combined Proteomics and Transcriptomics: Investigating the Bat-Virus Relationship in Deadly Emergent Disease

The emergence of Hendra Virus in Australia in 1994 represents one of many lethal zoonotic infections to appear in recent years, alongside Ebola, Marburg and SARS viruses. This paramyxovirus causes severe disease in horses and transmission to humans leads to a mortality rate of 57%. Meanwhile, infection of its natural reservoir host, bats of the Pteropus genus (otherwise known as flying foxes), causes only subclinical disease. This bat-virus relationship is a characteristic feature of many emergent zoonotic infections. An understanding of this relationship would inform efforts to combat Hendra virus and, potentially, its fellow bat-borne zoonoses. Investigating this phenomenon is hindered by bats' status as non-model species with genomes that are not as well annotated as humans. This makes proteomic analysis of such species difficult, as a database of proteins that could be in a sample is required. This analysis aims to compare the response of human cells and cells of the black flying fox to Hendra Virus infection. This was achieved by using the Proteomics Informed by Transcriptomics technique to generate a protein database from sequenced mRNA that can be used to identify proteins in the sample. This method allowed the effect of infection on the abundance of over 3000 identified proteins to be observed over time. Analysis revealed an extensively different effect on the two cell lines, with dissimilar numbers of proteins increasing, decreasing or staying relatively stable in abundance following infection and a disparity in the abundance of proteins involved in apoptosis implying an induction of apoptosis in human cells.

Theme 1: Cancer, Immunology and Infection

27 Adam Brayne, Year 5, University of Cambridge

Evolution of Hepatitis E Virus (HEV): How HEV has been jumping between pigs and humans

Hepatitis E virus infects 14 times more people worldwide than Hepatitis A virus each year, with a high incidence in the developed world, including the UK (3-7). Its importance is being increasingly recognised in clinical practice, and in public health, with its incorporation into liver screens and increasing concern that it is being transmitted through the UK blood bank (2). There are four genotypes of HEV which differ in their distribution, virulence and host species (1, 4–6). Using the largest ever dataset and state of the art methods we characterise the evolutionary similarities and differences between these genotypes. We find evidence that the ORF2/ORF3 overlap region, a key region of the genome involved in host-pathogen interaction, is evolving differently in zoonotic compared to human-only genotypes. We postulate this belies the frequent jumps between pigs and humans in these genotypes, and the signal of positive selection represents a cyclical but ultimately futile effort to attain fitness in each species before jumping again.

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Authors: Adam Brayne , Simon Frost

Theme 1: Cancer, Immunology and Infection

28 Natalia Grolmusova, Year 4, Oxford University

Molecular characterisation of a novel regulator of p53 signalling using the CRISPR-Cas9 system

Tumour suppressor p53-binding protein 1 (53BP1) is a key player in DNA double-stranded break (DSB) repair, known to drive repair via classical non-homologous end-joining (NHEJ), while suppressing the homologous recombination (HR) pathway. However, 53BP1 was originally discovered in a yeast two-hybrid screen as a p53-binding protein and recently a short hairpin (sh)RNA barcode screen identified it as a mediator of cytotoxicity upon p53 stabilisation. In this study, TP53 and 53BP1 were targeted using the clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 nuclease system to generate a knockout background. The effects of the gene modifications on survival upon treatment with the p53-stabilising agent Nutlin-3 (N3), as well as the changes in the protein expression of the new cell lines were investigated. The 53BP1-targeted cell lines were also characterized at the genomic level. The results obtained suggest that 53BP1 contributes to the anti-tumour toxicity induced by N3 independently of its role in DSB repair, thus potentially playing an essential role in the regulation of p53-dependent responses. Investigation of the interaction between p53 and 53BP1 could bring more insight into the regulation of p53,possibly leading to novel anti-tumour therapies.

Theme 1: Cancer, Immunology and Infection

29 Rory Ormiston, Final Year, University of Southampton

The Role of ERAP1 in HPV associated cancers

Introduction: ERAP1 trims peptides to their final length before they are displayed on MHC I at the cell surface. SNPs in ERAP1 alter trimming function and are associated with autoimmune diseases and cancer. HPV has been associated with squamous cell carcinoma of the head and neck (SCCHN) and prognosis is dependent on tumour infiltrating lymphocyte (TIL) levels. SNPs in ERAP1 have been associated with HPV+ve SCCHN outcome, the mechanism behind this is yet to be investigated.

Methods: Eight patients with SCCHN were recruited,50% HPV+ve and 50% HPV-ve. ERAP1 sequences were analysed. Identified ERAP1 allotypes and allotype pairs were assessed for trimming ability using a T cell hybridoma and N-terminally extended model antigen AVIMK-SIINFEKL. Expression levels of different ERAP1 allotypes were compared.

Results:11 out of a possible 16 allotpes were identified; WT (13%), KR/QE (69%), KR/QE.2 (13%), WT(L727A) (6%). SCCHN patients who were HPV+ve were all homozygous for the KR/QE ERAP1 allotype. Five ERAP1 allotypes were analysed individually for trimming function of model antigen AVIMK-SIINFEKL. KR/QE and KR/QE.2 were found to be hypofunctional. Three allotype pairs were analysed for trimming ability; efficient ERAP1 allotypes were seen to improve the trimming profile of hypofunctional variants. Although expression was similar, KR/QE allotype was show to have the highest expression levels.

Discussion: ERAP1 is highly polymorphic, SNPs vary the function of ERAP1 allotypes. However, the function of allotype pairs is more physiologically relevant. In patients who have only hypofunctional homozygous ERAP1 the trimming profile of model antigen AVIMK-SIINFKL is reduced. This may be HPV applicable; if various ERAP1 allotypes under-trim HPV epitopes, MHC-peptide expression may be reduced which may reduce levels of TILs and reduce immune rejection of HPV+ve SCCHN. Clinically an ERAP1 screen for HPV+ve patients could identify those with high risk ERAP1 and appropriate treatment, possibly in the pharmacological manipulation of ERAP1 could follow. –

Authors: Rory Ormiston Emma Reeves Edd James

Theme 1: Cancer, Immunology and Infection

30 Sivesh Kathir Kamarajah, Year 4, Intercalation, University of Birmingham

Transcytosis of Vascular Adhesion Protein-1 (VAP-1) from Perictyes to Endothelial cells in Liver Disease

Introduction – Vascular Adhesion Protein-1 (VAP-1) promotes recruitment of immune cells to inflamed tissue. Under resting conditions VAP-1 is expressed at low levels on the hepatic endothelium (HSEC). During inflammation increased levels of VAP-1 are detected in the hepatic sinusoids despite expression of the protein in HSEC being refractory to cytokine treatment. We propose that HSEC can sequester soluble VAP-1 released/cleaved from the surface of hepatic pericytes (1-3) and present the protein at the cell surface (4) to promote the recruitment of inflammatory cells.

Methods Primary human HSEC were co-cultured with the human hepatic stromal cell line LX-2 that had been transfected to express a FLAG-tagged VAP-1 fusion protein (VAP-1-FLAG). The release and uptake of VAP-1 was studied by confocal microscopy following treatment with cytokines, proteinases or exogenous VAP-1.

Results Co-cultures of HSEC and LX-2 VAP-1-FLAG cells were viable and we were able to detect expression of both VAP-1 and the FLAG-tag by confocal microscopy. VAP-1 was present in vesicles in the transfected LX-2 cells and in membrane projections that were intimately associated with HSEC. The uptake of exogenously soluble VAP-1 by HSEC was promoted by the addition of a cytokine cocktail. The mechanism of release from pericytes remains unclear as a panel of proteinases failed to cleave VAP-1 from the surface of LX-2 cells.

Conclusions The uptake of VAP-1 by endothelial cells is regulated by the presence of proinflammatory cytokines with the potential to regulate inflammatory cell recruitment. Whether pericytes are the source of this soluble VAP-1 requires further investigation.

Theme 1: Cancer, Immunology and Infection

31 Tamsin McAllister, Year 6, Peninsula College of Medicine and Dentistry

Characterising the involvement of the Cre/Blr regulon in ß-lactam resistance in pathogenic Enteric bacteria

Introduction: CreBC is a two component regulator found in many enteric bacteria. It responds to carbon changes in the environment in Escherichia coli. A close homologue of this system in Aeromonas spp. controls the expression of ß-lactamase genes. CreBC has been found to have a significant role in ß-lactam resistance when activated in tandem with the AmpR regulated ß-lactamase AmpC in Pseudomonas aeruginosa. Methods: To determine whether CreBC has a role in ß-lactam resistance in enteric bacteria other than E. coli, reporters of CreBC activity from E. coli and Aeromonas spp. were used in the human pathogens Enterobacter cloacae, Citrobacter freundii and Klebsiella pneumoniae to attempt to select mutants with hyper-active CreBC systems and investigate the resulting phenotype. –

Results: It was not possible to select hyper-active CreBC mutants at a detectable frequency in the bacteria used. Despite a phenotype of decreased susceptibility to ß-lactam antibiotics in some 'mutants' selected, there was no indication of raised CreBC activity in association with this. –

Discussion: The results suggest that CreBC activation is less clinically relevant in terms of ß-lactam resistance in these enteric bacteria, even those with inducible AmpC ß-lactamases, than it is in P. aeruginosa.

Theme 1: Cancer, Immunology and Infection

32 Florence Edmond

An in vivo assay for Transcription Coupled Repair

Transcription coupled repair (TCR) is a sub-pathway of single stranded DNA repair which accounts for the preferential rate of repair of the coding strand, and simultaneously enables translocation to continue through protein roadblocks and oxidative lesions. Congenital failures within this pathway, as seen in Cockayne syndrome and Xeroderma Pigmentosum manifest as increased skin cancer risk, however the precise mechanism of rate enhancement is largely unknown. Conversely this system may be manipulated to increase cell survival in a wide variety of cancers. We developed a strand-specific assay suitable for genome-wide study of TCR, dependent on ligation of guided-oligonucleotides to 5' damage-specific ends. This technique was optimised on double strand and single strand breaks induced by restriction enzymes and confirmed by Sanger sequencing. We then extended ligation to damage-specific single strand breaks created by uvr proteins; the inherent TCR machinery in E.coli. We also applied this assay to test rates of repair in TCR incompetent E.coli cells in the study of mutation frequency decline protein; a protein involved in the coupling of stalled transcription complexes to the repair machinery. We present 5' ligation of guided-oligonucleotides to double strand breaks but not to single strand breaks induced by restriction digest. We also show 5' ligation to damage-specific single strand breaks created by uvr proteins at known lesions. We tested this method in vivo but no definitive results have yet been found. Nonetheless, our initial progress offers promise for the future use of 5' capture in the study of TCR.

Authors: Florence Emond, Demelza Ousbey, Nia Haines, Nigel Savery

Theme 1: Cancer, Immunology and Infection

33 Harriet Mitchell, Year 3, University of Bristol

Aiding understanding of female reproductive tract anatomy through the use of ultrasound imaging

Introduction: Reduction in teaching hours and limited guidelines has led to high variability in anatomical radiology teaching across UK medical schools. E-learning can provide additional cost-effective teaching but how best to design online tutorials for students still remains unclear.

Methods: Ultrasound was identified as the imaging modality students struggled most to interpret in the needs analysis, carried out prior to designing the tutorial. This study therefore looked into the role of MCQs in a novel female reproductive anatomy ultrasound tutorial. Second-year medical students were randomly allocated to control (n=56) or experimental tutorial (n=56). The experimental tutorial consisted of 18 embedded MCQs. Pre and post-tutorial questionnaires contained matched questions, which were analysed using mixed model ANOVA.

Results: Knowledge in female reproductive anatomy and ultrasound improved significantly by doing the tutorial ($P<0.001$). Controls improved by 3.5/14 (95% CI: 2.8 to 4.1) and those who had the tutorial containing MCQs improved by 3.7/14 (95% CI: 3.1 to 4.4). However there was no significant difference in improvement, between control and experimental groups. Type II error may have been present due to insufficient discriminatory potential of pre versus post-tutorial questionnaires. Student feedback indicated improved confidence at interpreting ultrasound imaging. The experimental group reported higher perceived female reproductive anatomy knowledge compared to controls (63% versus 46%). 87% and 91% of control and experimental students agree/strongly agree that the tutorial successfully delivered its learning outcomes. Clinical cases were rated as the most engaging aspect of the tutorial. Control and experimental students, recommended that less text and addition of ultrasound videos would improve the tutorial.

Conclusions and Discussion: This study provides an example of how e-learning can be used to successfully teach ultrasound to pre-clinical medical students. The exact role of embedded MCQs in online tutorials still remains to be optimised.

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Authors: Mitchell H, Alder D, Fulford A. –

Theme 1: Cancer, Immunology and Infection

34 Zain Nadeem Amir, Year 4, University of Bristol

Functionalising Stem Cells Using Protein Surfactant Bioconjugates

Introduction: The therapeutic potential of stem cell based regenerative medicines have been widely publicised and well established. However, the key limitations facing stem cell based therapies of central necrosis among large-scale tissue engineered constructs and lack of in vivo stem cell imaging, are preventing widespread clinical acceptance and advancement of the field(1, 2). These limitations can be overcome by functionalising stem cells. This involves the integration of exogenous proteins and their individual properties into the cells. Current mechanisms include gene manipulation, direct cell surface engineering and artificial membrane anchors(3, 4). However, these have their individual issues.

Methodology: An alternative approach was established by the Perriman group, involving chemical cationisation followed by electrostatic conjugation of proteins with anionic surfactants to form protein-surfactant bioconjugates. This was utilised to address the two stem cell limitations individually. To tackle central necrosis, mesenchymal stem cells (MSCs) were partitioned with myoglobin-surfactant bioconjugates, before undergoing osteogenic tissue engineering. Successful functionalisation was assessed histologically and through zeta-potential studies. To address the lack of in vivo stem cell labelling, MSCs were partitioned with the superparamagnetic magnetoferritin-surfactant bioconjugtes. Successful functionalisation was assessed using MACS Separation, Transmission Electron Microscopy and MTS cell-viability assays.

Discussion: Overall, the cationisation and conjugation reactions were found to successfully introduce alterations to the protein, which allowed successful cell membrane integration. The used of myoglobin to minimise central necrosis however, showed inconclusive results highlighting further work is needed. On the other hand bioconjugated magnetoferritin was able to successfully functionalise cells without cytotoxicity.

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Theme 2: Cardio-respiratory, Endocrine and Neuroscience

35 Sarah Stoll, Year 2, University of Bristol

Shear-Stress Regulated Cell-Cell Communication via MicroRNA in the Renal Glomerulus

Introduction: The glomerular filtration barrier is an essential feature of the Kidney and is in part composed of the Glomerular Endothelial Cells (GEnCs) and Podocytes. A lot of evidence has emerged on regulation of GEnCs by podocytes but less is known about the inverse relationship. We hypothesised that GEnCs release microRNAs which regulate podocyte gene expression. We thought this was a result of laminar shear stress (LSS) induced by blood flow.

Methods: Conditionally immortalised GEnCs and podocytes were cultured. The GEnCs were treated under static and chronic LSS conditions using an orbital shaker. A sample of the medium was sent to Cardiff for microRNA analysis and the rest was applied to the podocytes. The control condition involved endothelial medium from the bottle applied to the podocytes. After podocyte treatment RNA extraction, cDNA synthesis and qPCR was carried out. –

Results: There were significant differences for changes in gene expression in the podocytes for FOXO3, IRS1 and MMP3. IRS1 and FOXO3 were both increased significantly in chronic compared to static conditions, but interestingly the control was highest in FOXO3 and lowest in IRS1. MMP3 was significantly higher in chronic LSS than the control. Cardiff found MicroRNA-126 was significantly increased in chronic LSS compared to static conditions in the GEnC medium whilst microRNA-143/145 showed the opposite.

Discussion: MicroRNA-126 was thought to be responsible for IRS1 and FOXO3 gene expression changes whilst microRNA-143/145 was thought to be implicated in MMP3 gene expression changes. It would be interesting in the future to confirm this by doing a microRNA assay. In addition carrying out the experiment in diabetic conditions would be a way to identify if there are any changes that may be implicated in causing diabetic nephropathy.

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Author: Sarah Stoll, Year 2, University of Bristol
Supervisor: Dr Simon Satchell
PhD Supervisor: Dr Hesham E Hussein El Hegni

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

36 Daniel Potter, Year 4, Leeds University

Factors Associated with Medication Adherence and Mortality Following Myocardial Infarction: A Linked National Cohort Stu

Background: Following a myocardial infarction (MI) over half of patients may not take their medication correctly. Adherence to these medications is associated with reduced mortality. However, whether patient factors confound this relationship is presently unclear.

Aim: To evaluate the effect of patient factors on medication adherence and mortality following MI.

Methods: Prospective multi-centre cohort study linking longitudinal patient-reported data with baseline characteristics from the Myocardial Ischamia National Audit Project (MINAP) registry. Factors associated with medication adherence and mortality were quantified using univariate and multivariate regression.

Results: Cohort included 3343 patients diagnosed with MI between 2011 and 2013. Ninety-one percent of participants were classified as adherent to all five medications. Medication adherence was positively associated with older age and quitting smoking. Participants who regularly exercised following ST-segment elevated MI (STEMI) but not non-STEMI (NSTEMI) were more likely to be adherent to individual medications, most significantly to statins (adjusted odds ratio: 2.9 p=0.02), and all five medications (adjusted odds ratio: 6.2 p=0.03). Medication adherence was negatively associated with continuing to smoke and cardiovascular comorbidities. Seven percent of participants had died by the end of follow up. Mortality was positively associated with older age, smoking and comorbidities. Participants who regularly exercised were less likely to die following STEMI (adjusted hazard ratio: 0.19 p=0.03) and NSTEMI (adjusted hazard ratio: 0.56 p=0.05).

Conclusions: Medication adherence and mortality following MI were associated with age, smoking, exercise and cardiovascular comorbidities. Future studies investigating the effect of medication adherence on mortality should account for these confounding factors.

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

37 Grace ME Pearson, Year 4, University of Bristol

Investigating the role of metformin in the prevention and treatment of diabetic nephropathy

Unable to attend to present

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

38 Perry Maskell, Year 3, UoB for Med, KCL for intercalation

Carbonic Anhydrase in the Enterosalivary Circulation of Dietary Nitrate

Background: Through participation in the Nitrate-Nitrite-NO Pathway, dietary nitrate supplementation (inorganic anion, NO3-) with beetroot juice has been shown to decrease blood pressure, inhibit platelets and mediate endothelial function in healthy volunteers.(1) The ubiquitous carbonic anhydrases, have been shown to play roles in various kinetic stages of the Nitrate-Nitrite-NO Pathway including the renal excretion of nitrate. However, the role of secretory salivary carbonic anhydrase (type VI) in nitrate handling has yet to be elucidated. We build upon unpublished data from this group which suggests carbonic anhydrase inhibition through acetazolamide decreases renal excretion of nitrate resulting in increased plasma [nitrate], yet results in a fall in plasma [nitrite]. We investigate the effect of acetazolamide on the enterosalivary circulation of nitrate as a possible explanation for this.

Method: In a double-blind, placebo-controlled crossover study design with 8 healthy volunteers over 7 hours, we studied the effects of acetazolamide (vs. placebo), following a nitrate load in the form of beetroot juice, on the amounts of nitrate and nitrite in saliva, plasma, and urine. In addition we measured exhaled NO (FENO-) and blood pressure. –

Results: Acetazolamide increased the production of salivary nitrate and saliva volume. However, the production of salivary nitrite was decreased by 18.7 µmol/h (95% Confidence Intervals 5.9 to 31.5). This coincided with a slight increase in blood pressure compared to placebo (P=0.045). Conclusion: The inhibition of salivary carbonic anhydrase with acetazolamide interrupts the lingual reduction of nitrate to nitrite in the enterosalivary circulation, explaining the decreased plasma [nitrite] seen in the previous study, and limiting the ability of the nitrate load to lower blood pressure in the current study. Complete analysis of plasma and urine samples of this study is needed to help confirm this physiological effect.

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Theme 2: Cardio-respiratory, Endocrine and Neuroscience

39 **Pierre Vila**, Year 6, University of Oxford

Structural and functional MRI abnormalities in methcathinone abusers with a parkinsonian syndrome

Background: Over the last decade, a distinctive extrapyramidal motor syndrome has been described in a number of young abusers of the psychostimulant drug methcathinone. It is attributed to deposition of contaminant manganese, as reflected by characteristic globus pallidus hyperintensity on T1-weighted MRI. As methcathinone abusers present with a complx motor neurological profile, we investigated whether the syndrome is associated with changes in structure and functional, questions not explored by previous studies.

Methods: We have investigated changes in brain grey matter morphometry and functional connectivity in intravenous methcathinone abusers (n=12) compared to matched control subjects (n=12) using T1-weighted structural and resting state functional MRI. MRI data acquired in Estonia and Oxford was analysed using tools from the FMRIB Software Library (FSL).

Results: Voxel-based morphometry showed patients to have significant grey matter loss ($p<0.05$) bilaterally in the putamina and caudate nucleus. Resting state functional MRI analysis showed increased functional connectivity within the motor networks of patients ($p<0.05$), particularly within the right primary motor cortex.

Conclusions: The manganese exposure associated with prolonged methcathinone abuse results in widespread structural and functional changes affecting both subcortical and cortical grey matter and their connections. Our results illustrate that in intravenous methcathinone/manganese abusers affected by the characteristic movement disorder, there is a more widespread pattern of grey matter damage than demonstrable by conventional imaging techniques.

Authors: Julius Juurmaa Ricarda AL Menke Pierre Vila (Presenting) Andreas Muursepp Tiiu Tomberg Pilvi Ilves Mait Nigul Heidi Johansen-Berg Michael Donaghy Charlotte J Stagg Ainars Stepens Pille Taba

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

40 **Akriti Nanda**, Year 2, University of Oxford

Morphological plasticity in lactotroph, gonadotroph and FS cells in sheep kept under different photoperiods

In seasonal mammals photoperiod regulates prolactin secretion, such that prolactin plasma concentrations peak during the summer months and are lowest during the winter. In sheep, a short day breeder, circulating prolactin has important inhibitory actions on pituitary gonadotrophs and hypothalamic GnRH release. The exact cellular mechanisms which account for the chronic hypersecretion of prolactin during summer is not known, but evidence supports an intra-pituitary mechanism regulated by melatonin which acts at MT receptors in the pars tuberalis to stimulate release of neurokinin A. Receptors for neurokinin A are localised to folliculo-stellate (FS) cells which produce paracrine factors that influence PRL release. This study examined the effects of different photoperiod on the ultrastructure of the lactotroph, gonadotroph and FS cell populations and their distribution in LP compared to SP. Sheep were housed in artificial light dark cycles, either 8:16 h light / dark cycle for short photoperiod (SP) or 16:8 h light / dark cycle for long photoperiod (LP) for 4 weeks. Ovine pituitary glands were collected and prepared for quantitative electron microscopy. It was found that lactotrophs in LP had greater cytoplasmic area ($P<0.05$), and showed a reduced number of PRL granules per micron cytoplasmic area compared to lactotrophs in SP (NS). In LP secretory granules showed a polarisation towards a neighbouring capillary and lactotrophs were more frequently found adjacent to a capillary compared to SP. There was no significant difference in the number of lactotrophs adjacent to FS cells in LP vs SP. Gonadotrophs in SP were observed in greater numbers ($P<XX$) and showed greater amounts ($P<XX$) of dilated rough endoplasmic reticulum consistent with greater amounts of LH and FSH synthesis and release in SP vs LP. FS cells in SP were frequently observed in clusters, contained more rough ER and chromatin was pale (transcriptionally active) in contrast to FS cells in LP displaying greater amounts of dense heterochromatin (transcriptionally inactive). These findings demonstrate plasticity in the morphology of lactotrophs, gonadotrophs and FS cells with photoperiod which reflect changes in PRL and LH secretion.

Authors: Nanda A, Loudon A, McNeilly AS, Christian HC

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

41 Samuel Lawday, Year 6, University of Southampton

Remote ischaemic preconditioning in children with congenital heart disease and healthy volunteers: A Pilot Study

Background: As the mortality of children born with congenital heart disease (CHD) decreases, these patients are now dealing with the consequences of ischaemic-reperfusion injury associated with the cardiopulmonary bypass used during surgery. Remote ischaemic preconditioning (RIPC) offers protection against this through sequential arterial inflow occlusion/reperfusion in a peripheral vascular bed, however the biological mechanisms involved remain ill defined. Microcirculatory blood flow (MBF) and gas-phase chemiluminescence, amongst other techniques, were used to assess the efficacy of published RIPC protocols and the role of nitric oxide (NO), respectively, in this setting.

Methods: 4 Children with CHD and 12 healthy adult volunteers were enrolled and subjected to a total of three 5-minute sequential cuff inflations targeted at 15mmHg above the systolic blood pressure (SBP) on the proximal arm separated by 5 minutes of reperfusion. MBF and temperature on both arms were measured using laser doppler, alongside oxygen saturation (SO2) and oxygenated haemoglobin (oxyHb) levels distal to the cuff (Moor Instruments UK).

Results: MBF, oxyHb and SO2 were significantly reduced during ischaemia. However, there were no reactive increases in MBF, SO2 and oxyHb after the occlusion and no contralateral vasodilation (a suggested marker of protection in RIPC). A significant decrease in circulating nitrite/nitrate was seen in adult healthy volunteers, however no changes in NO metabolites were apparent in children with CHD.

Summary and Conclusions: RIPC may offer a simple non-invasive mechanism to improve outcomes after surgery for children with CHD. We have established a simple method for testing the efficacy of arterial inflow occlusion as part of the RIPC protocol. MBF monitoring allowed us to show that although ischaemia was achieved using inflation pressures 15mmHg above SBP, this pressure may be insufficient for RIPC to be effective in all settings. Our preliminary results may potentially explain negative trial data reported by others. Further studies would seem to be required to investigate sufficient cuff inflation pressures for optimal protection by RIPC.

Authors: Lawday S, Glaedowe F, Poudevigne M, Fernandez BO, Minnion M, Clough G, Pappachan J, Feelisch M

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

42 Sebastian Green, Year 4, University of Bristol

Mapping out recognition memory circuits of the rat.

Recognition memory loss is very common, particularly in Alzheimer's disease. The hippocampus (HPC), perirhinal cortex (PRH) and medial prefrontal cortex (mPFC) are all implicated in recognition memory (1-2). This study used dual retrograde fluorescent labelling in rats (n=13) to map out part of the neural circuit between these anatomical structures for the first time. The density of retrogradely labelled neurons from the mPFC and PRH was recorded across subregions of the hippocampal formation. This allowed projections from the HPC to the PRH and mPFC to be recorded. Neurons from the HPC predominantly originated in the CA1 and subiculum subregions, almost exclusively travelled in the ipsilateral cerebral hemisphere, and seldom bifurcated to both the PRH and mPFC. Overall, hippocampal projections were stronger to the mPFC than the PRH. This anatomical variation suggests there is functional segregation for recognition tasks within the hippocampal formation. Furthermore, the absence of bifurcating neurons to both the mPFC and PRH implies the existence of separate anatomical streams, which may carry different types of recognition information. Neurodegeneration of the projections involved in this neural circuit may predict recognition memory loss in humans. Understanding these pathways may aid future therapeutic measures.

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Authors: Green, Sebastian (Student) Supervisors: Warburton, EC. Barker, G.

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

43 Laura Allen, Year 4, Leeds University

Factors Affecting Exercise Capacity In Diabetic Heart Failure Patients

Background: Exercise intolerance is a key feature of chronic heart failure (CHF). CHF patients with concomitant diabetes (CHF-DM) have heightened exercise intolerance, poorer prognosis and worse symptoms. Causative mechanisms may be impaired ventilatory, cardiac or skeletal muscle function. We prospectively assessed factors affecting exercise capacity in CHF and CHF-DM.

Methods: Stable CHF (n=33) and CHF-DM (n=33) patients with left ventricular systolic dysfunction (ejection fraction (EF) <50%; NYHA class I-II; optimal device and medical therapy), were matched for age (mean±SD: 76±7 yr), weight (85±13 kg), height (1.72±0.06 m), systolic function (EF: 38±11%) and diastolic function (EA ratio 0.9±0.2). They underwent peak cardiopulmonary exercise testing with breath-by-breath pulmonary gas exchange analysis. Exertional shortness of breath (S) symptoms were recorded using the standardized Borg 0-10 scale. Continuous variables were reported as means (SD) and analysed using ANCOVA, categorical variables were analysed using the chi-squared test. A p-value of < 0.05 was taken as significant.

Results: CHF-DM had reduced exercise capacity (pVO2 13.9±4.3 v 17.5±5.9 ml/kg/min; p=0.01) and lower exercise time (354±209 v 511±250s; p=0.01). Cardiac and ventilatory responses did not differ: Heart rate rise (44±5 v 46±4 bpm; p=0.21), Ve/VCO2 (37.2±9.4 v 39.5±10.5; p=0.35), peak respiratory frequency (31.7± 6.7 v 31.1± 7.6 breaths/min; p=0.76). Symptoms did not differ at baseline, peak or during exercise (Peak Borg S: 4±2 v 4±2; p= 0.73) The lactate threshold (LT) (9.86±0.27 v 11.26 ±0.32 L/min; p=0.48), time to LT (358 ± 92.58 v 393 ± 203.94 s; p=0.22) and the respiratory compensation point (RCP) (12.77±0.37 v 14.37± 0.45 L/min; p=0.64) did not differ.

Conclusion: Exercise capacity is reduced in CHF-DM subjects matched for age, BMI and cardiac function. There are no differences in symptoms of breathlessness, Ve/VCO2 slope or respiratory rate. However, LT and time to LT is unchanged, despite lower exercise time overall. Thus, there is an inability to tolerate exercise beyond the LT. This is likely due to altered skeletal mitochondrial function in the context of concomitant diabetes. –

Authors: Allen LN, Jamil HA, Gierula J, Paton M, Garnham J, Bowen S, Kearney MT, Witte KK

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

44 **Zara Dyar**, Year 3, University of Bristol

The effect of cAMP analogues on calcium transients in rat cardiomyocytes

Unable to attend to present

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

45 **Mariyam Saviour**, Year 5, Imperial College, London

Smooth pursuit eye movement as a sensitive marker of traumatic brain injury

Unable to attend to present

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

46 Lauren Passby, Year 5, University of Oxford

Role of Lrrk2 in human pluripotent stem cell-derived macrophages

Introduction: Parkinson's Disease (PD) is the second most prevalent neurodegenerative disease, and can be either familial or sporadic in origin. Leucine-rich repeat kinase 2 (LRRK2) has been identified as the mutated gene at the PARK8 locus, which is responsible for around 10% of familial cases of PD, and around 2% of sporadic cases. Despite this knowledge, little is known about the physiological role of Lrrk2 and its interactors, though expression of Lrrk2 has been shown in DA neurons, leukocytes, and other cell types.

Methods: Induced pluripotent stem cells (iPSCs) derived from control fibroblasts and PD-patient fibroblast samples were differentiated into macrophages following a verified protocol. Expression of Lrrk2 was induced by IFN, ?, before Lrrk2 and any bound interacting proteins were immunoprecipitated. Interacting proteins were identified through MS, and further evidence of interaction examined through Western blot (WB) analysis of immunoprecipitate samples.

Results: Pooling of 3 PD patient-derived iPS macrophage cell lines facilitated proteomic analysis that showed a number of interactors. Of these, Stomatin-like protein 2 was found to interact with Lrrk2 and to be specifically immunoprecipitated with the protein. Vimentin and beta-actin-like protein 2 may also interact with Lrrk2, though there was discrepancy between MS and WB findings.

Discussion: The proteins identified as fall within the functional categories of phagocytosis and cytoskeletal rearrangement. Lrrk2 's interaction with proteins within these categories is well-documented1-2, though interactions between Lrrk2 and Stomatin-like protein 2 and beta-actin-like protein 2 have not previously been reported. Development of Lrrk2-/, cell lines and mCherry-tagged Lrrk2 will allow for discrepancies between MS and WB findings to be overcome, and for the Lrrk2 interactome to be better understood. By better understanding the role of Lrrk2, it will be possible to better understand its role in the pathophysiology of PD.

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Authors: Passby, Lauren Cowley, Sally Browne, Cathy Thomas, Benjamin James, William

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

47 Edward Caplan, Year 4, University of Bristol

The Effects of Locomotor Training and Epidural Stimulation on Perineuronal Expression in Spinal Contused Rats

This study was designed to explore molecular effects of two types of rehabilitative therapy, Locomotor Training (LT) and Epidural Stimulation (ES), on two indices of neuroplasticity at two lumbar spinal levels following Spinal Cord Injury (SCI). LT and ES are theorised to modulate Perineuronal Net (PNN) expression to increase neuroplasticity and improve motor patterns. Cartilage link proteins (Crtl-1) are crucial components of PNNs, determining their formation and expression. Six adult rats underwent T10 thoracic contusions, followed by random assignment to one of three groups: LT, ES or Control. LT involved distributed treadmill step-training. ES involved continuous stimulation at L2. Treatments were delivered 5d/wk (20mins/d) for 8 weeks. Caged controls were housed in similar conditions. The results of this study suggest that LT can modulate PNN expression as measured by Crtl-1 staining intensity. This effect is more apparent at L5 than L2, which is more distal to the contusion. The effects were not observed for ES. This research adds to literature on PNN expression as a function of two rehabilitation techniques and highlights the importance of examining multiple indicators of PNN expression. Furthermore, the specific spinal segment, particularly with respect to contusion proximity, appears to be an important mediating variable in the regulatory process and warrants further investigation. The results underscore the complexity in the way in which PNNs are regulated in response to SCI rehabilitation.

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

48 Amy Huxtable, Year 6, Peninsula Medical School

Biventricular strain response to exercise in healthy adolescents – a novel study.

Objective: To investigate biventricular global longitudinal strain (GLS), left ventricular (LV) global circumferential strain (GCS) and right ventricular (RV) area in systole (RVAreas) and diastole (RVAread) at rest, during exercise and recovery in healthy adolescents.

Study design: Resting echocardiograms were performed to establish resting data. Participants (n=15, mean age 13.87 y) were tested to volitional exhaustion on a semi-recumbent cycle ergometer. Workload commenced at 0W, increasing in 25W increments every three minutes. Echocardiograms were performed half-way through each stage and at two and six minutes post-exercise.

Results: A significant increase in LVGLS between 50W and six minutes recovery (6minRec) was found (-18.14 ±4.34 versus 12.27 ±2.32 %; P=0.003). Significant differences were found for LVGCS between rest and 50W (-22.13 ±3.48 vs27.76 ±3.91 %; P=0.001), 50W and two minutes recovery (2minRec) (27.76 ±3.91 vs 23.55 ±4.19 %; P<0.001) and 50W and 6minRec (27.76 ±3.91 vs22.49 ±4.62 %; P<0.001). RVAreas revealed significant differences between rest and 2minRec (9.73 ±2.55 vs 7.18 ±2.03 cm2; P<0.001), rest and 6minRec (9.73±2.55 versus 7.36±2.23 cm2; P=0.004) and 50W and 2minRec (8.99 ±2.20 versus 7.18 ±2.03 cm2; P=0.005). No significant differences were found for RVGLS or RVAread; P>0.05.

Conclusion: This study has shown significant differences in ventricular deformation and right ventricular area between rest, 50W and post-exercise stages. This suggests that there is a valid area of research that needs to be explored with larger samples. Larger samples may provide normal reference values for clinicians when faced with deterioration in their patients. Given that the paediatric literature base is limited, it may be beneficial to establish which parameters are the most important for a paediatric population so research can become focused. Identifying ventricular dysfunction earlier would allow for appropriate management steps to be put in place for those with congenital heart disease.

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

49 Alexander Rutherford, Year 4, Cardiff University

mTOR Pathway Analysis in Rett Syndrome

Introduction: Rett Syndrome (RTT) is a neurodevelopmental X-linked disorder caused by mutations in the methyl CpG-binding protein 2 (MeCP2) gene. RTT presents with delayed development and loss of acquired skills and autonomic function, caused by abnormal dendritic and synaptic organisation, arborization and function. MeCP2 causes transcriptional activation or repression in neurons through interpretation of epigenetic methylation signals. The effect on individual pathways in RTT neurons is not clear and could elicit a therapeutic target. The mammalian target of rapamycin (mTOR) pathway regulates cell growth and protein synthesis, and abnormal function is strongly implicated in RTT pathology. This study analysed components of the two complexes in the mTOR pathway, mTORC1 and mTORC2, and the main downstream effectors at the mRNA and protein level in mice and iPS neurons to examine effects on the mTOR pathway and to determine the viability of iPS neurons as a RTT model.

Methods: RNA and protein levels were examined through quantitative-PCR and western blotting. Phosphorylation status was analysed to compare pathway activation. This study compared the mTOR pathway in a mouse model with a human iPS cell model at the RNA and protein level.

Results: No changes were observed to mouse mRNA and protein levels in the mTOR pathway. The human mTOR pathway was found to be upregulated in mutant iPS neurons, with hyperphosphorylation of PRAS40, an inhibitor of mTORC1 when non-phosphorylated, and rpS6, a downstream target of mTORC1 and a regulator of ribosomal biogenesis. However, results were found to be inconsistent with existing literature showing mTOR pathway downregulation in mutant neurons. Results indicated wild type iPS cell line contamination during development with mutant neurons, however this would not account for the differences with existing literature observed.

Discussion: Given the contrasting effects MeCP2 mutations cause in mouse and human iPS neurons, this study does not validate use of iPS cells as a RTT model. This contradicts existing literature, which concludes that mTOR pathway downregulation is centrally implicated in CNS malfunction in RTT neurons. Nevertheless, these results are interesting for their contrast with existing literature, and for the differences observed between both mouse and iPS neurons. –

Authors: Rutherford, A.J, Millar, D.

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

50 Benjamin Smeeton, Graduated from University of Exeter

Depletion of the Meckel-Gruber syndrome protein TMEM67 (meckelin) results in failure of ciliogenesis

Unable to attend to present

Theme 2: Cardio-respiratory, Endocrine and Neuroscience

51 **Shyama Chadha**, Year 6, Queen Mary University of London, Barts and The London School of Medicine

Improving Reprogramming Efficiency and Neuronal Differentiation of Down Syndrome Induced Pluripotent Stem Cells

Background: Protocols for developing human induced pluripotent stem (hiPS) cells from blood cells and skin fibroblasts have been optimised. However, keratinocytes offer a less invasive cell source. This project aims to optimise the protocol for the generation of integration-free iPS cells from keratinocytes and to optimise the differentiation protocol of neural progenitor cells (NPCs) from iPS cells.

Methods: Keratinocytes were isolated from hair follicles and underwent lipid-mediated transfection. Reprogramming factors were delivered via three integration-free episomal plasmids, with EGFP used as a visual marker. Variations in transfection conditions and tissue culture conditions were trialled, with the percentage of GFP positive cells monitored for transfection efficiency. Neuronal induction and expansion was carried out following the Life Technologies protocol (publication number: MAN0008031). NPCs were stained for neural stem cell and pluripotency markers (Nestin, Sox2, Oct4, Sox1 and Pax6) and compared with previously derived NPCs.

Results: The optimal transfection condition achieved a transfection efficiency of 21.2%±3.1 (mean percentage of GFP positive cells ±SD). However, no iPS cell colonies were derived. The newly trialled NPC protocol resulted in cells comparable to those previously derived in the lab that had been successfully reprogrammed into functional neurons and used for disease modelling.

Conclusion: A successful lipid-mediated transfection protocol was optimised as well as an efficient and less labour intensive NPC differentiation protocol. Enhancement of reprogramming efficiency is yet to be achieved.

Theme 3: Epidemiology, General practice and Global Health

52 **Madiha Majid**, Year 5, University of Birmingham

Young People who Self Harm: a Prospective One-Year Follow-up Study

Introduction: Almost half of all suicides have a history of self-harm, rising to two thirds for younger people [1]. Whilst a history of self-harm is a significant predictor for completed suicide, repetition and requiring emergency care have also been implicated to have a significant link[2]. Receiving a psycho-social assessment following presentation to emergency services with self-harm significantly reduces the risk of repetition, yet repetition remains high[3]. Little evidence exists to evaluate repetition in young people, their care provision and subsequent service engagement following self-harm, forming the rationale for this study. The aims of this study were to explore repetition, service provision and service engagement following presentation of young people to emergency services with self-harm.

Methods: 969 patients who presented to accident and emergency services after self-harm and received a psycho-social assessment were followed up prospectively for a period of one year. A psychosocial assessment was provided by a specialist psychiatric liaison service known as Rapid Access, Interface and Discharge. Data on rates, method, clinical history, initial service provision, engagement and repetition (defined as re-presenting to emergency services with further self-harm) were gathered from comprehensive electronic records.

Results: Young people were less likely to repeat self-harm; 23.6% of young people compared to 29.7% of those aged 25 years and above re-presented to accident and emergency with an episode of self-harm (?2 = 3.87, p=0.05). Those who had experienced childhood sexual abuse, and had a psychiatric history were at a significantly greater risk of repetition (HR 2.74, CI 1.43-5.25, p=<0.01 and HR 2.62, CI 1.46-4.70, p=<0.01 respectively). Young people were more likely to receive self-help as their initial service provision, and less likely to receive acute psychiatric care and a hospital admission. There were no differences in engagement with services between young people and those aged 25 and above.

Discussion: Younger individuals may be less vulnerable to repetition, and are less likely to re-present to services with repeated self-harm. Whilst young people are less likely to be referred to psychiatric services, they do attend when referred. This may indicate missed opportunity for intervention.

References: [1] Cooper J, Kapur N, Webb R, Lawlor M, Guthrie E, Mackway-Jones K, Appleby L (2005) Suicide after deliberate self-harm: A 4-year cohort study. Am J Psychiatry 162:297-303 [2] Kapur N, Cooper J, King-Hele S, Webb R, Lawlor M, Rodway C, Appleby L (2006) The repetition of suicidal behavior: a multicenter cohort study. J Clin Psychiatry 67:1599-1609. doi: 10.4088/JCP.v67n1016 [3] Cooper J, Steeg S, Bennewith O, Lowe M, Gunnell D, House A, Hawton K, Kapur N (2013) Are hospital services for self-harm getting better? An observational study examining management, service provision and temporal trends in England. BMJ Open 3:e003444-2013-003444. doi: 10.1136/bmjopen-2013-003444 –

Authors: Madiha Majid, Maria Tadros, George Tadros, Swaran Singh, Matthew R. Broome, and Rachel Upthegrove

Theme 3: Epidemiology, General practice and Global Health

53 **Maria Tadros**, Year 6, University of Birmingham

Self-Harm in Minority Ethnic Groups: presentation, intervention and outcome

Background: The UK has one of the highest rates of self-harm in Europe, and also an increasingly diverse population. However, there remains little research on self-harm in minority groups, many of whom have poor access to mainstream mental health services. This paper explores the influence of ethnicity on presentation, repetition, service intervention and patient engagement following self-harm presenting to accident and emergency (A&E).

Methods: Data from 893 sequential presentations to the Rapid Assessment Intervention and Discharge (RAID) Service in Birmingham were included from electronic data records and followed prospectively for 12 months. Descriptive statistics and chi-squared values were used to describe the socio-demographic features, precipitants and clinical features of the self-harm act. Multinomial and binary logistic regression were used to identify predictors of service offered to patients, how likely they were to engage with services, and how this differed based on ethnicity. Results Black and Minority Ethnic (BME) groups under-present with self-harm to A&E and show more characteristics typically considered 'low risk'; living with others, being in education and having no known psychiatric diagnosis. BME patients who have a diagnosis are more likely to have psychosis than White groups. Despite this BME groups receive significantly less specialist management following self-harm, and if referred are more likely to disengage with services subsequently. However no significant differences are found in rates of re-presentation with self-harm.

Discussion: Consideration for previously undiagnosed mental illness, including psychosis, should be part of psychiatric assessment tailored to BME groups following self-harm. BME patients do not re-present more frequently, despite non-attendance in clinical services, and this may reflect an enduring lack of engagement. Improvements in culturally accessible liaison and acute services that engage patients with treatment are needed when help seeking, such as presentation to A&E, does occur. Future studies should focus on more detailed cultural and religious factors, including qualitative research to capture subjective perspectives and explore reasons for referral decisions and lack of engagement.

References: Hawton, K., Bergen H, Casey D, Simkin S, Palmer B, Cooper J, Kapur N, Horrocks J, House A, Lilley, R. (2007) Self-harm in England: a tale of three cities. Social psychiatry and psychiatric epidemiology. 42:513-521. Singh S, Islam Z, Brown L, Gajwani R, Jasani R, Rabiee F, et al. (2013) Ethnicity, detention and early intervention: reducing inequalities and improving outcomes for black and minority ethnic patients: the ENRICH programme, a mixed-methods study. Programme Grants Appl Res. 1(3). Raleigh VS, Irons R, Hawe E, Scobie S, Cook A, Reeves R, Petruckevitch A, Harrison J (2007) Ethnic variations in the experiences of mental health service users in England: results of a national patient survey programme, Br J Psychiatry. 191:304-312.

Authors: Maria Tadros, Madiha Majid, George Tadros, Swaran P Singh, Mathew R. Broome, Rachel Upthegrove

Theme 3: Epidemiology, General practice and Global Health

54 Anna Taylor, Year 4, University of Bristol

Healthcare provision for adults with CFS/ME and psychiatric co-morbidities: a comparison of the UK and USA

Introduction: Chronic Fatigue Syndrome (CFS) or Myalgic Encephalomyelitis (ME) has a prevalence of at least 0.2-0.4%1. Co-morbid anxiety and depression are common2-3. However, there is little literature on whether differences in healthcare provision between the UK and USA health systems alter detection and treatment. We aimed to examine disparities in access and delivery of healthcare between patients with CFS/ME and psychiatric co-morbidities in the UK and USA, hypothesizing that different healthcare systems affect healthcare provision.

Methods: The interview sample was recruited from the pool of healthcare professionals partnering with CDC in conducting the Multi-Site Clinical Assessment of CFS Study, which involves seven CFS-specialist clinics across the USA. Thirteen semi-structured interviews were conducted with healthcare professionals, including doctors, physician's assistants, a nurse practitioner, a research coordinator, a clinical exercise physiologist, and a clinical neuropsychologist. Audio recordings were transcribed, anonymised, and analysed thematically using techniques of constant comparison. Analysis compared provision in the USA with data existing from the UK, commenting on whether access and delivery of healthcare differs between systems.

Results: Two superordinate themes emerged. Participants commented on the difficulties patients face when accessing specialist services, identifying factors such as poor recognition in primary care, unstructured referral pathways and few services. Participants also talked about managing psychiatric co-morbidities. Subthemes included divergent treatment philosophies, beliefs about risk factors for co-morbidities, barriers to accessing mental healthcare, and managing patient expectations.

Discussion USA clinicians report problems with healthcare provision for adults with CFS/ME, such as lack of recognition of CFS/ME in primary care. This is consistent with UK data; ethnic minorities in both the UK and USA face additional barriers to care. Poor access may be due to a lack of health insurance coverage. This differs from the UK, which has universal healthcare coverage and NICE treatment guidelines. In the USA, divergent treatment philosophies of specialist services and no cohesive treatment protocol for CFS/ME and psychiatric co-morbidities may affect detection and the management of patients with CFS/ME and anxiety or depression.

References: 1. NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE. (NICE). (2007). Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalomyelopathy): diagnosis and management of CFS/ME in adults and children. London: National Institute for Health and Clinical Excellence 2. NATER, U.M., LIN, J.M., MALONEY, E.M. (2009). Psychiatric co-morbidity in persons with chronic fatigue syndrome identified from the Georgia population. Psychosomatic Medicine. 71:557-565 3. CELLA, M., WHITE, P.D., SHARPE, M., CHALDER, T. (2013). Cognitions, behaviours and co-morbid psychiatric diagnoses in patients with chronic fatigue syndrome. Psychol Med. Feb;43(2):375-80 –

Author: Miss Anna Taylor Dr Esther Crawley Dr Jin-Mann Lin Dr Elizabeth Unger

Theme 3: Epidemiology, General practice and Global Health

55 Benjamin Clayton, Year 5, Peninsula College of Medicine & Dentistry

Motivation for studying medicine: Assessing the similarities between UK and Ghanaian medical students

Introduction: Countries around the world experience challenges in ensuring equal distribution of health workers. For countries faced with this problem, there are many benefits to international co-operation. Before this can occur however, there needs to be an understanding of the homogeneity of medical students between countries. This paper assesses the similarities in motivation to study medicine between medical students from the United Kingdom and Ghana.

Methods: A survey previously performed on fourth year Ghanaian students was reproduced with medical students in the United Kingdom. Students were asked to record their motivation for studying medicine, opinions on future career (general practice for United Kingdom students and a rural position for Ghanaian students) and basic demographics. The results were compared between the two cohorts using Fisher's exact test.

Results: 302 Ghanaian and 78 United Kingdom medical students completed the survey. 63.5% and 75.0% of students were classified as intrinsically motivated in Ghana and the United Kingdom respectively. Apart from parental education status, student demographics were broadly similar. Within the United Kingdom cohort, 30.1% of students considered it likely that they would work in general practice in their future careers.

Conclusion: Medical students are similarly motivated between the two countries. This suggests that greater co-operation may be possible when tackling difficulties in human resources for health. This is especially relevant for the United Kingdom, as the level of students predicting a career in general practice in this study remains well below the national target.

Theme 3: Epidemiology, General practice and Global Health

56 Shanze Naseem Ashai, Year 2, University of Bristol

Suspected dengue patient presenting with West Nile Virus in Sindh, Pakistan: a case report

The co-occurrence of symptoms such as fever, drowsiness, and, a singular seizure, confirmed meningioencephalitis in a 57-year-old female patient from Karachi, Pakistan – a city where the dengue virus is endemic – these symptoms therefore are attributed to dengue fever itself and the patient is diagnosed with such. Here, we present a case, where the cause of these symptoms turned out to be due to exceptionally rare West Nile Virus, whose presence was confirmed by the use of immunochromatographic testing. West Nile Virus has not been adequately researched in this region and, so, we present the first known incidence of the virus in Karachi since 1988. In epidemiological terms, this case highlights the need for conclusive genetic testing of all incoming presumed dengue patients, which can be used as a means to shed light onto the existence of other arboviral conditions in Pakistan.

Authors: Shanze Ashai Erum Khan Joveria Faruqi

Theme 3: Epidemiology, General practice and Global Health

57 **Avgi Loizidou**, Year 4, University of Bristol

The effect of Internal Migration on Childhood Development a systematic review

Unable to attend to present

Theme 3: Epidemiology, General practice and Global Health

58 Hannah Leaver, Year 6, University of Southampton

Educating medical undergraduate students on the promotion of physical activity: a questionnaire based study

Introduction: Physical inactivity is one of the major public health challenges of the 21st century. 1,2) costing the NHS £8.2 billion annually. 3) Only one third of UK adults adhere to current PA guidelines. 4) Physicians are being increasingly called upon to prescribe PA to patients, however a paucity of exercise medicine teaching in the medical curriculum prevents medical students from acquiring the essential knowledge and skills to promote PA to patients. 5, 6) It is therefore very important to teach medical students about PA, however, few medical schools do so and the most effective teaching method to do so has yet to be established.

Methods: The aim of this study was to evaluate the effectiveness of the Faculty of Sport and Exercise Medicine (FSEM) booklet on exercise prescription, designed for medical students. Clinical medical students with no previous SEM experience were invited to complete a 17-item online validated questionnaire prior to and after receiving the FSEM booklet. The questionnaire assessed knowledge regarding the importance of PA in disease prevention and management and students' confidence advising patients about PA. Additionally, it gauged the students' ability to apply their knowledge to case scenarios. Results: In total, 79 and 25 medical students completed the questionnaire at baseline and follow up, respectively. Participants agreed that PA is important in preventing and managing disease, and is an important part of a doctor's job. Students' confidence in their knowledge of the Chief Medical Officers' (CMO) guidelines and their confidence in advising patients about PA significantly increased after using the booklet ($p<0.05$, calculated by Wilcoxon signed rank test).

Discussion: Use of the booklet effectively improved students' confidence in advising patients about PA and in their knowledge of the CMO guidelines. These improvements are encouraging and may initiate improved and increased PA counselling amongst tomorrow's doctors. This resource is a cost and time effective method of teaching medical students about PA. However, further research is required to find the optimum method of improving medical students and healthcare professionals knowledge and delivery of advice on PA. Word count = 334

References: 1. Blair Steven N. Physical inactivity: the biggest public health problem of the 21st century. British journal of sports medicine. 2009;43(1):1-2. 2. World Health Organisation. Global recommendations on physical activity for health. Geneva: WHO, 2010. 3. Office for National Statistics. Health survey for England. In: Rachel Craig, Jennifer Mindell, Hirani V, editors. Volume 1, Physical Activity and Fitness. London; 2009. 4. Health Department of. Start active, stay active. London: 2011. 5. Weiler Richard, Chew Stephen, Coombs Ngaire, Hamer Mark, Stamatakis Emmanuel. Physical activity education in the undergraduate curricula of all UK medical schools. Are tomorrow's doctors equipped to follow clinical guidelines? British journal of sports medicine. 2012. 6. Pate R. R., Pratt M., Blair S. N., Haskell W. L., Macera C. A., Bouchard C., et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. Jama. 1995;273(5):402-7.

Authors: Hannah Leaver, Dr Manuela Angioi, Dr Patrick O'Hal

Theme 3: Epidemiology, General practice and Global Health

59 **Ffion James**, Year 4, Cardiff University

A Critical Analysis of Factors that Influence Emergency Medicine Consultants in their Careers.

Unable to attend to present

Theme 3: Epidemiology, General practice and Global Health

60 Joanna Miles, Year 4, University of Bristol

Causes of a change in joint angle variability of the upper limb in the female overarm lacrosse shot

Very little research so far has considered the biomechanics involved in the sport of women's lacrosse. Within this study, the basic biomechanical elements occurring in the upper limb during a lacrosse shot were examined and considered in relation to participant playing level, stick offset and previous injury status. Five female participants undertook a series of lacrosse shots with three different sticks, two straight and one offset. Motion data was collected using CODA (frequency: 100Hz) and video capture in order to calculate joint angle and joint angle variability data. Joint speeds increased in a proximal to distal pattern across segments in all participants, suggesting a basic coordination pattern is present throughout the lacrosse shot. Elite players showed reduced variability in joint angles at the ball release point towards the end segments of the movement whilst novice players recorded higher levels of variability of release point joint angles throughout all segments. However, both groups showed an overall reduction in variability in joint angles at release as segments become more distal. Ball release times were consistently maintained across all three sticks with the most experienced participant showing the earliest ball release times. The offset stick caused a statistically significant reduction in stick release angle variability when compared to the other sticks. Previous shoulder and clavicle injury caused a reduction in variation across all joints whilst maintaining a constant stick release angle variability and ball release time. In conclusion, none of the theories surrounding variability are exclusively conclusive as to how variability changes with playing level. Instead, aspects of each are required to work in unison to create the pattern of variability shown.

Network and WiFi

Staff and Students from Eduroam Organisations

The University is part of the Eduroam federation which provides reciprocal access to wireless internet for staff and students from other Eduroam institutions.

Visitors from an Eduroam organisation should find their laptops and mobile devices automatically connect to wireless at Bristol, provided that they have been correctly configured for Eduroam in advance at the home organisation.

If there are any problems, requests for technical support must be directed to the home organisation and cannot be handled by IT support at Bristol.

The Cloud WiFi

Staff, students and visitors capable of using Eduroam should do so in preference to The Cloud. If you still want to use The Cloud then connecting is easy.

You simply need to connect to 'The Cloud' wireless signal in the WiFi settings of your device

Once connected, open your web browser and refresh the page

You will see The Cloud landing page and here you can login/register with your account

Once logged in you're good to go! Please note that web based apps will not work until the connection has been established and you have signed in successfully via your web browser.

Tweet us!

Want to meet like-minded people and fuel the discussion rolling long after the event? Tweet us with #INSPIREIntercalatorsConference …We look forward to seeing your messages on the day!

Travel Information

Conference Venue

Lecture Theatre 1 & 2
School of Chemistry
Cantock's Close, Bristol, BS8 1TS

[Marked in dark red on the attached map – final page]

Rail: Bristol Temple Meads Railway Station is 15 minutes away by car although traffic can be heavy which will increase your travel time. Regular buses and taxis pick up from the train station. The 520, 8 or 9 bus will take you in walking distance of us.

Bus: The number 8 and number 9 buses run to and from Bristol Temple Meads train station and run every 10 minutes in peak times. The nearest stop is on Queens Road, near Sainsbury's supermarket (turn right on exiting Wills Memorial building and walk 200m). The journey should take about 20-30 minutes. www.firstgroup.com/bristol-bath-and-west

Road: From the M5 join the M4 at junction 15, then from the M4 join the M32 at junction 19. Follow the M32 straight into the city centre and continue straight to the A4044 (Cabots Circus a shopping centre should be on your left). At the roundabout take the second exit onto Marlborough Street and after the Bristol Royal Infirmary and Childrens' Hospital continue along Park Row turning right at the garage into Woodland Road.

Parking: Parking in Bristol is limited and we advise that you research the location of a car park before setting off. There are chargeable multi-storey car parks about ten minutes' walk from the conference venue, as shown on the attached map.

There is very limited free on-street parking on 'St Michael's Park' (BS2 8BW). There are also a handful of university staff spaces in the car park behind the Chemistry building on Medical Avenue (BS2 8BB). Please note that both areas are open to members of the public on Saturdays, thus spaces are not guaranteed.

[Marked in light blue on the attached map – final page]

Coach: National express runs services to Bristol bus station where you can walk up the hill to us (it is quite a steep hill) or take a short taxi ride.

Taxis:	V Cars	0117 925 2626
	City Link Taxis	0117 925 1111
	Streamline Taxis	0117 926 4001

Information for Presenters

Oral presentations

Your talks will be 10 minutes long (each sessions will be strictly chaired). Talks should be prepared with Powerpoint and will be loaded onto the lecture theatre PCs. Please submit talks by 19th October so we can upload them and check that they work. The chair will invite questions from the audience after each talk so be prepared to be quizzed. We will also invite the audience to vote on each presentation / question session as part of the prize assessments (scores will not be visible to the audience).

Poster presentations

Please prepare posters in portrait A0 format (or landscape <1m wide) with text large enough to be read from a distance of 2m. Posters should not be so densely detailed that they are difficult to read - they are a graphical communication medium. You will be expected to be at your poster from 1pm when there will be a facilitated poster discussion organised by theme. Please prepare a 1 minute brief synopsis of your project and expect to be questioned about the details. The prizes will be decided by the theme facilitators.

Acknowledgements

Meeting Organisation

This meeting is the product of an ongoing collaboration between the INSPIRE committees of the Universities of Bristol, Cardiff, Exeter and Plymouth. Particular thanks go to Abla Hatherall, Kay Russell and Elle Chilton-Knight for organising the event and to the Deans of the Faculties of Biomedical and Health Sciences for their ongoing support (fiscal and moral). We also thank all of the speakers, session chairs, facilitators and programming committee for their time and enthusiasm.

Funders

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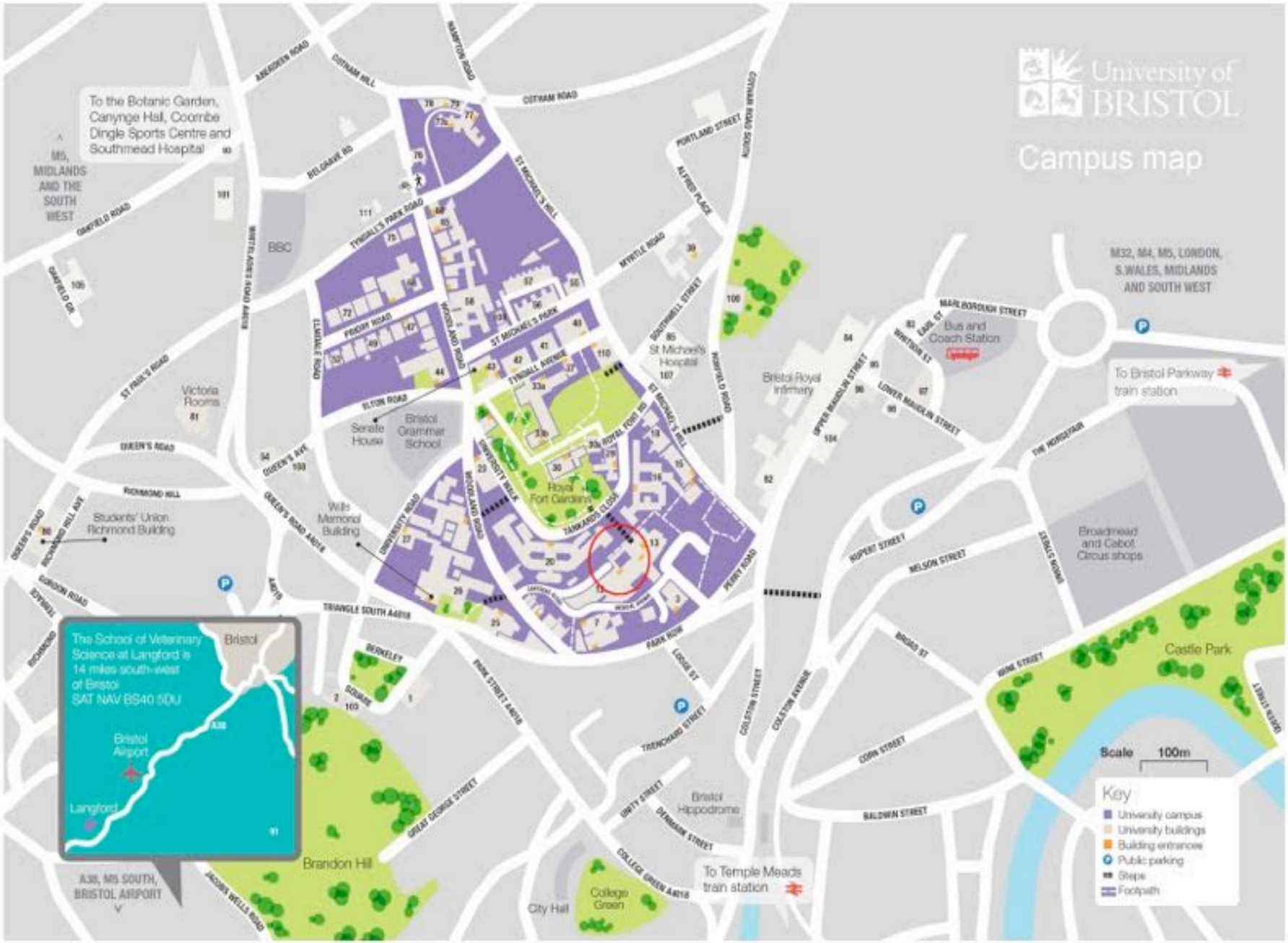
University of BRISTOL
Campus map
To the Botanic Garden, Canynge Hall, Coombe Dingle Sports Centre and Southmead Hospital
M5, MIDLANDS AND THE SOUTH WEST
M32, M4, M5, LONDON, S.WALES, MIDLANDS AND SOUTH WEST
To Bristol Parkway train station
To Temple Meads train station
Bus and Coach Station
Bristol Royal Infirmary
St Michael's Hospital
BBC
Victoria Rooms
Senate House
Bristol Grammar School
Royal Fort Gardens
Wills Memorial Building
Students' Union Richmond Building
Broadmead and Cabot Circus shops
Castle Park
Bristol Hippodrome
City Hall
College Green
Brandon Hill
The School of Veterinary Science at Langford is 14 miles south-west of Bristol
SAT NAV BS40 5DU
Bristol
Bristol Airport
Langford
A38, M5 SOUTH, BRISTOL AIRPORT
Scale 100m
Key
University campus
University buildings
Building entrances
Public parking
Steps
Footpath