New Horizons in Medical Research

A Scientific Conference organised by the School of Medicine Research Committee, UCC

Thursday 10th December 2015

Main Atrium, Western Gateway Building, UCC

Free registration on site from 8am

A TRADITION OF INDEPENDENT THINKING

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

New Horizons Research Conference 2015

Western Gateway Building G14
Thursday 10th December 2015

UCC
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

New Horizons
Medical Research Conference 2015

Welcome Message from the School of Medicine Organising Committee

Dear Friends and Colleagues,

On behalf of the school's organising committee, it is a great pleasure to welcome you all to the New Horizons Medical Student Research Conference 2015. This research showcase will provide an opportunity to enjoy presentations on a diverse range of clinical and translational medical research projects completed across the School. It will enable students and staff to discuss the latest research in medical sciences, with contributions from staff, undergraduate and postgraduate scientists at the forefront of developments in their areas. The program includes a stimulating mixture of oral and poster presentations, in addition to plenary lectures by prominent clinician scientists and academic staff.

We hope that all todays' participants, students and staff enjoy the conference programme, as well as the hospitality of UCC during the event.

Yours sincerely,
School of Medicine, Research Committee.
http://www.ucc.ie/en/medical/research/horizon/

Acknowledgements

The Dean of the School of Medicine, Professor Mary Horgan, and the Research Committee would like to take this opportunity to thank the New Horizons organising committee*, in particular, Shauna Breen, Kevin Laatz, Moya Revins and Rose Walsh. In addition, we would like to thank the sessional Chairs, Professor Geraldine Boylan, Dr. Elizabeth Brint, Professor Jonathan Hourihane, Dr. Niall Hyland, Dr. Justin McCarthy and Professor Mike Prentice.

We would also like to thank the judges of the oral presentations, Dr. Paula O'Leary and Dr. Mark Rea; and the poster judges, Dr. Orla Barry, Dr. Patricia Fitzgerald, Dr. John MacSharry, Dr. Yvonne Nolan, Dr. Gerard O'Keeffe, Dr. Colm O'Tuathaigh and Dr. Gabriella Rizzo.

A poster prize has been kindly sponsored by the CRF-C UCC, for which the School is grateful.

* Dr. Liam J. Fanning
Dr. Bridget Maher
Dr. Colm O'Tuathuaigh

Time	**New Horizons in Medical Research Conference 2015** **Schedule at a Glance** ****Key note speakers: Biographies, pictures and abstracts present**
08:00	Free registration commences
08:00	Hanging of posters in the main atrium WGB
08:55	Opening message by Dr. Liam Fanning, Chair School of Medicine Research Committee
	Session 1
	Chairs: Professor Geraldine Boylan & Dr. Justin McCarthy
09:00	Dr. André Toulouse:** Department of Anatomy and Neuroscience, UCC. "*Cellular models for the study of neurogenerative disease*"
09:25	Short Communications: O1. Dr. Anand Gururajan, Dept. of Anatomy & Neuroscience, UCC. *"The microRNA, let-7b, is a trait biomarker of treatment-resistant depression"* O2. Miss Jacklyn McCarthy, National Suicide Research Foundation, UCC. *"Profile of patients presenting to emergency departments with high-risk suicidal behaviour"* O3. Ms. Sandra Yeomans, School of Biochemistry and Cell Biology, UCC. "*Peripheral Akt activity: a potential biomarker for Parkinson's disease"*
09:55	Professor Patricia Kearney:** Department of Epidemiology and Public Health, UCC. "*The Burden of Diabetes in Ireland*"
10:20	Short Communications: O4. Dr. Susan Joyce, School of Biochemistry and Cell Biology and APC Microbiome Institute, UCC. *"Microbial interactions at the Gut interface"* O5. Dr. Fiona Fouhy, Teagasc Food Research Centre. *"Altered gut microbiota in stable patients with cystic fibrosis (CF) compared to controls and its relationship with intravenous (IV) antibiotic usage and lung function"* O6. Miss Clara Seira-Oriach, APC Microbiome Institute, UCC. *"Microalgal Omega 3 polyunsaturated fatty acids (PUFAs) effects on cognition, sociability, depressive-like behaviour and brain fatty acid composition in C57BL/6 mice"*
10:50	COFFEE and Viewing of Posters in Atrium.

	Session 2
	Chairs: Dr. Elizabeth Brint & Dr. Niall Hyland
11:15	Professor Mary Cahill:** Department of Haematology, CUH. "*Translation research in Haematology*"
11:40	Short Communications: O7. Dalyia Benjamin, Cork Cancer Research Centre, UCC. *"Investigation into the role of autophagy in differentiation in leukaemia"* O8. Miss Louise Daly, School of Nutritional Science, UCC. *"Sarcopenia, Myosteatosis & Weight loss: Negative Prognostic Indicators in Patients with Foregut Cancers"* O9. Dr. Kashif Ali Khan, UCC and CUH. *"The design and validation of a novel semiautomatic lung navigation platform"*
12:10	Dr. Sharon McKenna:** Cork Cancer Research Centre and Department of Biochemistry, UCC. *"Autophagy and cancer".*
12:35	Short Communications: O10. Miss Amruta S. Naik, Department of Medicine, UCC. "*Mutations of the immunodominant epitopes lead to humoral immune escape of Hepatits C Virus"* O11. Dr. Caitriona Hickey, Department of Microbiology, UCC. *"Hepatitis E Virus Infection in Ireland"*
12.55	LUNCH and viewing of posters. Poster judging.
	Session 3
	Chairs. Professor Jonathan Hourihane & Professor Mike Prentice
14:00	Dr. Gerard Clarke:** Department of Psychiatry and Neurobehavioural Science, UCC. "*The Biological Burden of Stress: Focus on Serotonin Synthesis and Tryptophan Metabolism*"
14:30	Short Communication: O12. Dr. Carol Ní Chaoimh, School of Food and Nutritional Sciences, UCC. *"Cord blood leptin and gains in body weight and fat mass during infancy"* Two Short Invited Communications: O13. BT Young Scientist 2014 winners – Ms. Eimear Murphy and Mr. Ian O'Sullivan, Colaiste Treasa, Kanturk, Co. Cork *" Potential causes of hazardous drinking in teenagers"* O14. Poster Winner of Atlantic Corridor Medical Research Conference Limerick - Donnchadh O'Sullivan *"Basehunter- a bacterial based DNA detection"*
15:05	Professor Gene Dempsey:** Department of Paediatrics and Child Health, UCC and CUH. "*Enhancing intubation skills in neonatal care*"
15:35	**Prize-giving.** Professor Mary Horgan. Dean, School of Medicine, UCC
15.45	**Meeting close:** Professor Mary Horgan. Dean, School of Medicine, UCC

Index

Biographies, pictures and abstracts for key note speakers in Sessions 1-3

SESSION 1:

Dr. Andre Toulouse
Department of Anatomy and Neuroscience, University College Cork
"Alternative ribosomal translation as a pathological mechanism in polyglutamine neurological disorders."

Dr. André Toulouse received a BSc degree in Biology from Université Laval (Québec, Canada) in 1991. He developed his expertise in the cellular and molecular biology of diseases by completing a MSc (1993) and a PhD (1998) in Molecular Biology at Université de Montréal (Montréal, Canada). His interest in Neuroscience led him to undertake post-doctoral work with Dr Guy Rouleau in the Centre for Research in Neuroscience at McGill University (Montréal, Canada) where he also worked as a research associate in the Neurogenetics Laboratory. His research areas included the identification and cloning of genes involved in neurodevelopmental disorders and the development of cellular models of neurodegeneration. In 2003, he moved to University College Cork to pursue post-doctoral work on the molecular biology of neurotrophic factors in the laboratory of Dr Aideen Sullivan in the Biosciences Institute. Dr Toulouse was appointed as College Lecturer in Clinical Anatomy and Principal Investigator in the Department of Anatomy and Neuroscience in September 2005.

His research is focused on the development of cellular models for the study of the molecular mechanisms of neuroprotection and neurodegenereation, with a particular emphasis on Parkinson's disease and the polyglutamine disorders. His work has been funded through personal fellowships from the Fonds pour la formation des chercheurs et l'aide à la recherche and the Fonds de la recherche en santé du Québec as well as research grants from the Health Research Board of Ireland and the Irish Research Council for Science, Engineering and Technology.

Abstract:
Alternative ribosomal translation as a pathological mechanism in polyglutamine neurological disorders.
André Toulouse and Ingrid Lager Gotaas
Department of Anatomy and Neuroscience, University College Cork

The polyglutamine disorders are a group of heterogeneous late-onset neurodegenerative disorders characterized by the expansion of a CAG trinucleotide repeat in the causative gene, the accumulation of insoluble protein material and premature neuronal cell death. Examples of these diseases include Huntington disease and the Spinocerebellar ataxias (SCAs). Recent work has provided support for several mechanisms that may account for

neurodegeneration in these disorders but no unifying mechanism has emerged yet. We have previously demonstrated that in SCA3 the expanded CAG tract is prone to frameshifting that may lead to the production of polyalanine-containing proteins. In order to further document the occurrence of frameshifting, assess its role in cell toxicity and understand its mechanism, a cellular model was established. We show that this phenomenon results from ribosomal slippage towards the –1 frame leading to the production of polyalanine proteins. We also show that ribosomal frameshifting depends on the presence of long CAG tracts and that polyalanine frameshifted proteins are more toxic than their polyglutamine counterparts, possibly contributing to pathogenesis. Finally, we present evidence that ribosome-interacting drugs can modulate -1 frameshifting, representing a possible therapeutic target for these disorders.

SESSION 1:

Professor Patricia Kearney
Department of Epidemiology and Public Health, University College Cork
"*The Burden of Diabetes in Ireland*"

Professor Patricia Kearney obtained a medical degree from University College Cork in 1998, graduating first in her class. She completed training in internal medicine in Ireland and the US. She was awarded a Fulbright Scholarship to undertake a MPH in Tulane University School of Public Health and Tropical Medicine and she subsequently completed a PhD in Public Health. In 2003 she was awarded a Wellcome Trust Cardiovascular Research Initiative Junior Research Fellowship to work as a Clinical Research Fellow at the University of Oxford. She worked at the Clinical Trial Services Unit & Epidemiological Studies Unit and her work focused on tabular and individual patient data meta-analyses. In 2007 she was awarded a Beeson Fellowship (NIH funded career development award) to work on TILDA, the Irish Longitudinal Study on Ageing and during her fellowship she worked as a Visiting Assistant Professor at the Centre of Aging and Population Health at the University of Pittsburgh as well as a Clinical Research Fellow in Trinity College Dublin and University College Cork. In 2008 she was appointed as Senior Lecturer in Public Health in University College Cork. Her research interests are in primary and secondary prevention of traditional risk factors for cardiovascular disease, lifecourse epidemiology and clinical trials. She is the Irish lead PI for TRUST, an EU funded FP7 clinical trial in subclinical hypothyroidism in healthy older adults. She leads a Health Research Board funded Interdisciplinary Capacity Enhancement (ICE) award that is utilizing data from 9 Irish observational studies to look at lifestyle transitions across the lifecourse. She is a member of the national steering committee for TILDA and chairs the cardiovascular working group. She has over 155 publications, including over 50 articles in peer reviewed international journals with approximately 17,000 citations, a h-index of 22 and an i-10 index of 33. She has generated €5.5 million in research grant funding since her appointment to UCC in 2009 and supervises a multi-disciplinary research team of 15 including research nurses, clinical fellows, post-doctorates and research students and she also supervises 10 PhD students. In 2013 she was one of six recipients nationally of the prestigious HRB Research Leader Award to undertake a project on a population approach to the prevention and control of diabetes. She was also appointed as a Research Professor in UCC.

Abstract:
Burden of Diabetes in Ireland

The prevalence of diabetes is increasing worldwide. Diabetes is a significant cause of blindness, non-traumatic lower limb amputations, end-stage renal disease and cardiovascular disease. Similar to other countries, Ireland does not have a national diabetes register or universal data-capture system to monitor the burden of type 2 diabetes and related complications. The aim of the HRB Research Leader Award is to develop a population approach to the prevention and control of diabetes. The programme of work

includes prevalence and trends in diabetes and its complications, modelling of the costs of diabetes, an evaluation of the national clinical programme in diabetes and the development of a technology based physical activity intervention in pregnant women at risk of gestational diabetes. A systematic review of published studies on the prevalence of diabetes and its complications has been completed and data from the Irish Longitudinal Study on Ageing (TILDA) has been analysed to estimate prevalence, complications and health service use due to diabetes. The prevalence of diabetes in Ireland among people aged 50 years and over is 8.4% (95% CI 7.8-9%) and is higher among men (10.3% [95% CI 9.4-11.2%) than women (6.6% [95% CI 5.9%-7.5%). The overall prevalence of microvascular complications is 26% (95% CI 22.4-30.0%) and of macrovascular complications is 15.1% (95% CI 12.2-18.4%). Among TILDA participants, diabetes was independently associated with more frequent use of GP - IRR 1.3 (95% CI 1.2-1.4), OPD – IRR 1.3 (95% CI 1.1-1.6) and ancillary services – IRR 1.6 (95% CI 1.4-1.9).

SESSION 2:

Professor Mary Cahill
Department of Haematology, Cork University Hospital
"Translation research in Haematology"

Professor Mary Cahill graduated from UCC in 1986. Having completed two years training in CUH she took up a training post in haematology in Leicester and then in the Royal London. During her time in London she completed two years of full time research on platelets and platelet function in myeloproliferative disorders, culminating in an MD award from the University of London.

She left London in 1997 to become the first (and only) Consultant Haematologist in the Mid Western Health Board providing service to Nenagh, Ennis and St John's hospitals as well as the Mid Western Regional Hospital (now University Hospital Limerick-UHL). She gained funding from the HRB for the clinical trials unit in University Hospital Limerick.

She moved to Cork University Hospital in 2004 to commence a full time position as Clinical and Laboratory Haematologist in CUH and Kerry General Hospital. Once in CUH where she continued her interest in clinical trials. She combines her full time clinical post with ongoing collaborative research, now focusing on autophagy in leukaemia with her colleague Dr Sharon McKenna in Cork Cancer Research Centre (CCRC). Drs Cahill and McKenna have co-supervised two medical doctors carrying out research and both are likely to be future clinician scientist leaders in haematology in the future.

She also has complimentary research interests in health care delivery and diagnosis. Currently she is involved in a large study on the diagnosis of pre-myeloma and myeloma in collaboration with Epidemiology and Public Health in UCC, thereby providing further links between CCRC and other UCC Departments. She is currently supervising a HRB funded Sphere Scholar carrying out research in this area.

CCRC and the department of Haematology, in which Mary has recently become a clinical Professor (2014) have strong links with Prof Caitriona O'Driscoll in the School of Pharmacy, facilitating further outreach for CCRC and fostering joint research on novel methods of therapeutics involving siRNA in leukaemia cells.

In 2015, she was awarded a SFI/ICS grant, in collaboration with colleagues in NUIG and TCD, to establish an all Ireland phase one clinical trials network. The research is linked to National Cancer Registry enhanced data collection and with additional funded enhanced bio-banking for blood cancers. This initiative, will allow for further blood cancer related research to be rooted in CCRC with on-going opportunities for national collaboration with NUIG and TCD.

Prof Cahill is the current chair of the curriculum committee in the Medical School in UCC and She has a major interest in teaching medical, nursing and science students in UCC.

Abstract :
Translational research in Haematology in UCC

Background. Advances in the care of patients with haematological malignancy have proceeded rapidly in the last decade. This is exemplified by improved survival for patients with conditions such as multiple myeloma and chronic myeloid leukaemia, where the advent of improved therapy led to dramatic improvement in survival in the last decade. In the case of CML the survival curve shows over 80% of patients alive at ten years on new therapies in contrast to a previous median survival of around three years. So, where do these therapies come from, how do they get to patients and what role does UCC play in these processes?

New drugs. Data from the FDA show a high level of expedited approval for drugs used in the care of the haematology patient worldwide. These approvals are the end process in a drug development pipeline that begins at the laboratory bench-often generated in academic institutions.

Data on autophagy and differentiation. Research carried out in UCC research feeds into transformative ideas cancer as a 'chronic disease'. One example of such an idea/process is autophagy. Our data on the process of autophagy shows that this complex cell survival mechanism may be harnessed to promote cell differentiation. Among the drugs which achieve this are high doses of vitamin A. Novel data on the master regulation of autophagy provides us with possible new therapeutic targets in this area which can be applied to the treatment of patients with acute leukaemia.

Data on the effects of siRNA therapy in human leukaemia cells. As an example of the therapeutic challenges presented by blood cancers, Prof Cahill will discuss the difficulties in eradicating the leukaemia stem cell which so frequently leads to relapse of acute leukaemia. Recent novel work in collaboration with the School of Pharmacy, demonstrates that intracellular drug delivery using siRNA targeted against a cancer oncogene in the leukaemia cell has been successful in reducing the transcription of oncogenic BRD4. This data in mice has just been substantiated in human leukaemia cells derived from patients with leukaemia.

Recent advances in clinical trials have seen phase 1b and phase 11 trials come closer together. Prof Cahill discuss how her success in securing collaborative SFI/ICS funding, to bring early phase clinical trials to University College Cork, will see patients benefiting from novel therapies and she will outline current progress in early phase clinical trials in CUH.

Population aspects and building infrastructural capacity for research in blood cancers. Finally, to secure the place of UCC as a vibrant hub for research into haematological malignancy in the next decade, a population prospective is vital. Prof Cahill will update the audience on SFI/ICS funded progress in bio-banking and enhanced cancer registration for blood cancers within a newly founded Blood Cancer Network Ireland (BCNI).The BCNI was launched on Nov 25th in NUIG (2015).

SESSION 2:

Dr. Sharon McKenna
Cork Cancer Research Centre and Department of Biochemistry, University College Cork

"Autophagy and cancer"

Dr. Sharon McKenna graduated from the University of Leicester in 1990 with an Honours Degree in Molecular Biology. She obtained her Ph.D at the Leukaemia Research Fund Laboratories, in the University of Wales, College of Medicine, Cardiff, UK in 1995. Following post-doctoral research at Cardiff and the Department of Biochemistry, UCC, Dr. McKenna was appointed as a Lecturer in the Department of Biochemistry, UCC in 1999 and was also group leader of the Signal Transduction Laboratory. In 2002, Dr. McKenna joined the Cork Cancer Research Centre (CCRC) as a Principal Investigator. She is responsible for the direction of the Autophagy program at CCRC. Her team is investigating how autophagy influences response to chemotherapy, how to improve therapeutic regimes with novel targeting strategies and how to predict response to therapy with novel bio-markers.

Abstract:
Autophagy in Cancer

Autophagy is a highly conserved catabolic process in which cells self-digest their organelles, protein aggregates and other macromolecules to generate monomers for new metabolic processes. As autophagy also clears damaged intracellular material, it can be protective against cancer. However, when a cancer is established, autophagy takes on new roles and helps cancer cells to survive in growth limiting conditions. Inducing excessive autophagy, leading to cell death can also be a major mechanism for killing cancer cells that cannot induce apoptosis. Many recurrent and metastatic cancers have lost apoptosis competency. At CCRC we are investigating how to manipulate autophagy to improve treatment of poor prognosis cancers. Oesophageal cancer is increasing in incidence in the Western world and five-year survival in Europe is only twelve percent. We have shown that chemo-sensitive oesophageal cancer cells exhibit apoptosis whereas chemo-resistant populations exhibit autophagy and Type II cell death. Cell populations that respond with autophagy are more resistant and recover following withdrawal of the chemotherapeutic agents. Inhibition of autophagy with siRNA targeted to autophagy regulators can reduce this recovery demonstrating the importance of autophagy for the survival of drug treated cells (1). We are currently developing novel combination strategies to impede the survival functions of autophagy in cancer cells and enhance Type II cell death (2). We have completed extensive pre-clinical testing and will test the first strategy in a clinical trial with oesophageal and colorectal cancer patients in Ireland (ICORG 11-32). We are also characterising genes and microRNAs that are differentially expressed in cells with apoptotic and autophagic treatment responses. This will deliver valuable insights into the molecular mechanisms that mediate treatment response. In addition, we have undertaken a retrospective analysis of oesophageal cancer patients treated in Cork and Dublin. We have shown that an autophagy

marker is highly predictive of outcome (3). We are currently screening other differentially expressed genes to look for additional bio-markers that are predictive of outcome. The overall aim of this group is to improve treatment protocols with new or existing compounds that can modulate autophagy and develop biomarkers to enable the selection of patients who need this treatment most.

1. O'Donovan TR, O'Sullivan GC, McKenna SL. Induction of autophagy by drug-resistant esophageal cancer cells promotes their survival and recovery following treatment with chemotherapeutics. Autophagy. 2011 May;7(5):509-24. PMID:21325880

2. O'Donovan TR, Rajendran S, O'Reilly S, O'Sullivan GC, McKenna SL. Lithium modulates autophagy in esophageal and colorectal cancer cells and enhances the efficacy of therapeutic agents in vitro and in vivo. PLoS One. 2015 Aug 6;10(8) PMID:26248051

3. Shereen El-Mashed, Tracey R. O'Donovan, Elaine W. Kay, Ayat R. Abdallah, Mary-Clare Cathcart, Jacintha O'Sullivan, Anthony O'Grady, John Reynolds, Seamus O'Reilly, Gerald C O'Sullivan and Sharon L. McKenna. LC3B globular structures correlate with survival in esophageal adenocarcinoma. BMC Cancer 2015, **15***:582*

SESSION 3:

Dr. Gerard Clarke
Department of Psychiatry and Neurobehavioural Science, University College Cork
"*The Biological Burden of Stress: Focus on Serotonin Synthesis and Tryptophan Metabolism"*

Dr. Gerard Clarke is a lecturer based in the Department of Psychiatry and Neurobehavioural Science and is also a faculty investigator in the APC Microbiome Institute. He graduated with a B.Sc (Hons) in Chemistry from the National University of Ireland, Galway followed by an M.Sc in Neuropharmacology from the same institution. He subsequently received a Ph.D (Department of Psychiatry) from University College Cork (UCC) in 2009. Gerard was a visiting scientist in the University of Mississippi Medical Centre in Jackson prior to working for a number of pharmaceutical companies in both Ireland and Australia, including Wyeth, Pfizer and 3M. This was followed by periods working as a postdoctoral researcher in the Alimentary Pharmabiotic Centre, as a Research Fellow in the Department of Psychiatry and as a lecturer in the Department of Pharmacology/School of Pharmacy prior to taking up his current position.

His laboratory takes a translational approach to the assessment of stress-related disorders such as depression and irritable bowel syndrome (IBS). This approach incorporates studies in both clinical populations and in animal models using early-life stress templates that produce specific disease phenotypes in adulthood. He is particularly interested in the advancing our understanding of how tryptophan degradation along the kynurenine pathway influences psychopathology and in evaluating interventions which can reverse such deficits. His current research program also focuses heavily on the impact of the gut microbiome on brain and behaviour across the lifespan. This is a rapidly expanding frontier area of research with enormous potential and one which is studied using the combined approach of germ-free animals, probiotic administration and antibiotic-induced dysbiosis. His research has been recognised internationally by travel awards from the European College of Neuropsychopharmacology (ECNP) as well as a prestigious career development award from the American Neurogastroenterology and Motility Society (ANMS) and a NARSAD young investigator award from the Brain and Behaviour Research Foundation. He has previously secured Health Research Board (HRB) funding to study the links between kynurenine pathway metabolites and cognitive dysfunction in IBS. He is also currently a principal investigator on a HRB funded study that seeks to define the biological burden of caregiving.

Abstract:
The Biological Burden of Stress and Inflammation: Focus on Serotonin Synthesis and Tryptophan Metabolism

Stress and inflammation have major mental health implications. The neurobiological basis for these effects may be underpinned by the converging impact on host tryptophan metabolism within the framework of the brain-gut-microbiome axis. Tryptophan is an essential amino acid and a precursor to both serotonin, a target of antidepressant medication, and a variety of neuroactive agents produced along the kynurenine metabolic pathway with relevance for cognitive performance such as quinolinic acid and kynurenic acid. The metabolism of tryptophan is heavily influenced by both glucocorticoids and immune parameters. We and others have recently demonstrated a key role for the gut microbiota in regulating both the availability and onward metabolism of tryptophan, giving this virtual organ a broad reach and the potential to impact on a spectrum of behaviours relevant to depression, anxiety, pain and cognition. Here, we discuss the implications of these findings in the context of irritable bowel syndrome, a prototypical stress-related microbiome-gut-brain axis disorder. Moreover, we evaluate the biological burden of family dementia caregiving and discuss a potential role for tryptophan metabolism in mediating the deleterious consequences of this chronic stressor. Integrating these findings with emerging research on the gut microbiome may provide the basis for novel management strategies for stress-related disorders.

SESSION 3:

Professor Gene Dempsey
Department of Paediatrics and Child Health, University College Cork and Cork University Hospital. "*Enhancing intubation skills in neonatal care*"

Prof. Eugene Dempsey, MB BCh BAO MD MSc FRCPI FFPAEDS

Professor Eugene Dempsey is a Consultant Neonatologist in the Cork University Maternity Hospital and Clinical Professor of Paediatrics and Child Health, University College Cork. He qualified from University College Cork, and completed subspeciality training in Neonatology at McGill University, Montreal. His MD was on Hypotension in the Preterm infant and he also has an MSc in Health care Ethics and Law. He is the Chief investigator for the HIP trial (Management of hypotension in the preterm infant), an FP7 funded project including centers from around Ireland, UK, Europe and North America. Prof. Dempsey is a Principal Investigator for Science Foundation Ireland and is a member of the Infant Centre at University College Cork, which has facilitated the development of strong multidisciplinary links with neurophysiology, computing and business informatics, all of whom are collaborating on a number of ongoing research projects, the theme of which involves improving outcome for the Preterm Infant.

Abstract:
Enhancing Intubation skills in neonatal care

Newborn care has witnessed significant progress over the last 30years. Survival at the limits of viability has increased substantially, with babies born at 23 weeks having favourable outcomes. I will describe the use of new manual ventilation devices, the use of carbon dioxide assessment, and video-technology to improve stabilization of the extreme preterm infant in the delivery room. Intubation remains a critical skill and can be technically very challenging, especially in very immature infants. I will describe the role of medical applications and video laryngoscopy to enhance trainees ability to acquire this technically challenging skill. I will describe the ongoing collaboration with the Tyndal Institute, funded via the TRAP Funding Scheme in the development of a neonatal video laryngoscope.

Oral Presentations:
G14 Western Gateway Building UCC

O=Oral Number

O	Author	Abstract Title
1	Gururajan, Anand *et al.*	The microRNA, let-7b, is a trait biomarker of treatment-resistant depression
2	McCarthy, Jacklyn *et al.*	Profile of patients presenting to emergency departments with high-risk suicidal behaviour
3	Yeomans, Sandra *et al.*	Peripheral Akt activity: a potential biomarker for Parkinson's disease
4	Joyce, Susan *et al.*	Microbial interactions at the Gut interface
5	Fouhy, Fiona *et al.*	Altered gut microbiota in stable patients with cystic fibrosis (CF) compared to controls and its relationship with intravenous (IV) antibiotic usage and lung function
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11	Hickey, Caitriona *et al.*	Hepatitis E Virus Infection in Ireland
12	Ní Chaoimh, Carol *et al.*	Cord blood leptin and gains in body weight and fat mass during infancy
13	Murphy, Eimear and O'Sullivan, Ian	Potential causes of hazardous drinking in teenagers
14	O'Sullivan, Donnchadh, *et al.*	Basehunter- a bacterial based DNA detection

O: 1

The microRNA, let-7b, is a trait biomarker of treatment-resistant depression

Submitting Author: Anand Gururajan

List of Authors: A Gururajan (1), KA Scott (1,2), GM Moloney (1,2), M Naughton (3), RM O'Connor (1), DM McLoughlin (5), J Dowling (4), G Shorten (4), A Walsh (4), L Scott (3), F Ismail (3), G Clarke (2,3), TG Dinan (2,3), JF Cryan (1,2)

(1) Department of Anatomy & Neuroscience, UCC
(2) APC Microbiome Institute, UCC
(3) Department of Psychiatry and Behavioural Neuroscience, UCC
(4) Department of Anaesthesia & Intensive Care Medicine, UCC, Cork
(5) Department of Psychiatry, Trinity College Dublin.

Discipline/Area: Department of Anatomy & Neuroscience, University College Cork

Abstract:
MicroRNAs are small non-coding RNAs that regulate gene expression and evidence implicates their involvement in the pathophysiology of depression (1). Altered peripheral expression of microRNAs in depressed patients lends support to the hypothesis that they can act as biomarkers of central pathology (2). These biomarkers would provide objective measures to improve diagnosis of depression and its subtypes, such as treatment-resistant depression (TRD), and refine treatment approaches. With ethical approval from the relevant committees we conducted experiments to identify microRNAs that were differentially expressed between 40 patients with TRD and 17 controls. We also determined whether microRNA expression in TRD patients was affected by treatment with ketamine or electroconvulsive therapy. Blood samples were taken at baseline in all study participants and in patients after treatment. Samples were then processed using microarray and PCR techniques to quantify microRNA expression levels. Results showed that the expression of miR-223 correlated with symptom severity as assessed by the Hamilton Depression Rating Scale but did not differ between TRD patients and controls and was also unaffected by treatment. In contrast, the expression of let-7b was significantly reduced in TRD patients compared to controls and remained unaffected by treatment. Bioinformatics analysis revealed 25 predicted targets of let-7b that are implicated in the PI3k-Akt-mTOR signaling pathway which is reportedly dysfunctional in depression (3). Our results suggest that let-7b is a trait biomarker of TRD. This work was funded by the Health Research Board (HRA_POR/2012/32).

1. O'Connor RM, Dinan TG, Cryan JF. Mol. Psychiatry. 2012; 17: 359-376
2. Issler O, Chen A. Nat. Rev. Neurosci. 2015; 16: 201-12
3. Kitagashi Y, Kobayashi M, Kikuta K, Matsuda S. Depress. Res. Treat. 2012; doi:10.1155/2012/752563

O: 2

Profile of patients presenting to emergency departments with high- risk suicidal behaviour

Submitting Author: Jacklyn McCarthy

List of Authors: Jacklyn McCarthy (1), Celine Larkin (1), Sara Leitao (1), Birgit Greiner (2), Eugene Cassidy (3), Ella Arensman (1,2)

(1) National Suicide Research Foundation, University College Cork
(2) Department of Epidemiology & Public Health, University College Cork
(3) Department of Psychiatry, University Hospital Cork

Discipline/Area: National Suicide Research Foundation, University College Cork

Abstract:
Self-harm is one of the strongest predictors of suicide123. Individuals who have engaged in high-risk suicidal behaviour share similar characteristics to those who die by suicide4. A limited number of studies have focused on high-risk suicidal behaviour5, especially in an Irish context.

As part of the larger SSIS-ACE study, presentations of high-risk suicidal behaviour were identified through the two Cork Emergency Departments from June 2014 to August 2015. A number of items were recorded including characteristics of the presentation and socio-demographic variables.

During the 15-month period 113 eligible patients presented to the EDs following an episode of high-risk suicidal behaviour. The majority of participants were male (65%). The average age across both genders was 35 years. There was a peak in those aged 30-35 years. Half of the presentations involved self-poisoning. Other common methods of self-harm included hanging (18%) and serious self-cutting or stabbing (12%). Despite having engaged in high-risk suicidal behaviour only 5% scored high (10-14) on objective suicide intent. Patients who had engaged in more lethal methods of self-harm such as carbon monoxide poisoning, strangulation and hanging scored higher overall.

This study is one of the first to examine Irish presentations of high-risk suicidal behaviour. Our findings suggest important similarities (gender) and differences (methods) between this group and those who die by suicide. Suicide intent varied by method. Despite having engaged in high-risk suicidal behaviour the majority of patients showed no significant physical injuries. This is especially relevant considering the poor survival rates of individuals who engage in attempted hanging, which is a frequently used method of highly lethal self-harm6.

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2. Owens, D., Horrocks, J., House, A. (2002). Fatal and non-fatal repetition of self-harm. *British Journal of Psychiatry, 181, 193-199.*
3. Hawton, K., Zahl, D., Weatherall, R. (2003). Suicide following deliberate self-harm: Long-term follow-up of patients who presented to a general hospital. *British Journal of Psychiatry, 182, 537-542.*
4. Hawton, K. (2001). Studying survivors of nearly lethal suicide attempts: An important strategy in suicide research. *Suicide and Life Threatening Behaviour, Vol 32 (supplement).*
5. Runeson, B., Tidemalm, D., Dahlin, M., Lichtenstein, P., & Langstrom, N. (2010). Method of attempted suicide as predictor of subsequent successful suicide: National long term cohort study. *British Medical Journal, 340:c3222.*
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(Funded by the Health Research Board, HRA-2013-PHR-438)

O: 3

Peripheral Akt activity: a potential biomarker for Parkinson's disease

Submitting Author: Sandra Yeomans

List of Authors: Yeomans SE(1), Manning E(2), Downer EJ(3), Timmons S(2), O'Neill C(1)

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(2) Department of Gerontology and Rehabilitation, UCC
(3) School of Medicine (Physiology), Trinity College Dublin

Discipline/Area: School of Biochemistry and Cell Biology, University College Cork

Abstract:
Defective PI3-kinase/Akt signaling is implicated in Parkinson's disease (PD) and our previous work has shown Akt activation is decreased in dopaminergic neurons in the brain in PD. We also demonstrated Akt activation is increased in the brain's "resident macrophages" microglia. The immune system is known to be involved in PD pathogenesis and Akt is a major regulator of both innate and adaptive immune cell functions. We therefore hypothesize there is a strong rationale for examining Akt activity in peripheral immune cells as a potential biomarker for PD.

Peripheral blood mononuclear cells (PBMCs), lymphocytes, CD14+ monocytes, M1 and M2 macrophages were prepared from (i) control non-PD individuals (n=10); (ii) individuals with PD not on medication for the disease (n=10) and (iii) patients with PD on dopamine modifying therapy (n=10). Akt activity and Akt isoform expression were examined in each cell type.

Results demonstrate a selective increase in Akt activation in M1 and M2 macrophages in both PD patient groups compared to matched controls, however, this attained significance in M1 macrophages in individuals newly diagnosed with PD that were not on any medication, $p = <0.05$.

Our results support the potential of the Akt system as a novel peripheral biomarker for PD, which we are presently investigating in larger patient groups. Follow up samples from our drug naïve cohort will determine if PD medications affect Akt activity which could be potentially used in the therapeutic monitoring of the disease.

We gratefully acknowledge ethical approval from the Clinical Research Ethics Committee of the Cork Teaching Hospitals and financial support from Atlantic Philanthropies and the Translational Research Access Programme (TRAP) UCC.

O: 4

Microbial interactions at the Gut interface

Submitting Author: Susan Joyce

List of Authors: Joyce SA(1,2), MacSharry J (1,3), Casey P (1,3), Kinsella, M(4), Murphy E(7), Shanahan, F(1,5), Hill, C (1,3), Gahan, C (1,3,6)

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Discipline/Area: APC Microbiome Institute, University College Cork

Abstract:
The key molecular mechanisms by which the gut microbiota can influence host energy metabolism and adiposity remain to be determined. Modification of bile has been postulated to act as a potential mechanism in this regard due to the local and systemic signalling properties of bile acids. We established a controlled expression system for the functional characterisation of bile metabolic enzymes in the murine gut. We show that bacterial bile salt hydrolase (BSH) mediates a microbe-host dialogue which functionally regulates host lipid metabolism and plays a profound role in cholesterol metabolism and weight gain in the host. Expression of cloned BSH enzymes in the GI tract of gnotobiotic or conventional mice significantly altered plasma bile acid signatures and regulated transcription of key genes involved in lipid metabolism, cholesterol metabolism, gastrointestinal homeostasis and circadian rhythm in the liver or small intestine. High-level expression of BSH in conventional mice resulted in a significant reduction of host weight-gain, plasma cholesterol and liver triglycerides demonstrating the overall impact of elevated BSH activity upon host physiology. In addition, BSH activity in vivo varied according to BSH allele group, indicating that subtle differences in activity can have significant effects on the host. In summary, we demonstrate that bacterial BSH activity significantly impacts upon systemic metabolic processes and adiposity in the host, and represents a key mechanistic target for the control of obesity and hypercholesterolaemia.

References should be quoted in the text as numbers in parentheses, and listed at the end of the abstract in the format outlined below (1,2).
1. Joyce et al., Proc Natl Acad Sci U S A. 2014;111(20):7421-6. doi:10.1073/pnas.1323599111
2. Joyce et al., Curr opinions in Gastro 2014. doi: 10.1097/MOG.0000000000000039
3. Joyce et al., Curr Opin Gastroenterol. 2014 Mar;30(2):120-7. doi: 10.1097/MOG.0000000000000039.

O: 5

Altered gut microbiota in stable patients with cystic fibrosis (CF) compared to controls and its relationship with intravenous (IV) antibiotic usage and lung function

Submitting Author: Fiona Fouhy

List of Authors: F. Fouhy (1), D.G. Burke (1,2), M.C. Rea (1,2), M. J Harrison (3,4), C. Stanton (1,2), O. O'Sullivan (1,2), D.M. Murphy (3,4), G. O'Callaghan (2,3,4), J. A Eustace (3), F. Shanahan (2,5), C. Fleming (4), M. Mc Carthy (4), C. Shortt (4), R. P. Ross (2,6), B.J. Plant (2,3,4).

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(2) APC Microbiome Institute, Cork, Ireland
(3) HRB Clinical Research Facility, UCC, Ireland
(4) Cork Cystic Fibrosis Centre, UCC, Cork University Hospital, Wilton, Cork, Ireland
(5) Department of Medicine, UCC, Cork,Ireland
(6) College of Science, Engineering and Food Science (SEFS), UCC, Cork, Ireland.

Discipline/Area: Teagasc Food Research Centre, Moorepark, Fermoy, Co. Cork, Ireland

Abstract:
CF is associated with an altered gut microbiota, compared with healthy controls. We present results from the largest CF gut microbiota study to date.

The gut microbiota of 43 stable adults with CF was compared to 69 age-matched controls. DNA was extracted from faecal samples and was sequenced using 454-pyrosequencing. Results were correlated with baseline % predicted FEV1 and total courses of IVs in the previous 12 months. Ethical approval was received from the Clinical Research Ethics Committee of the Cork Teaching Hospitals.

Significantly increased proportions of Firmicutes ($p=0.029$) and decreased Bacteroidetes ($p<0.001$) occurred in those with CF compared to controls. There were significant reductions in proportions of bacteria associated with gut health in those with CF, including decreased Faecalibacterium, Roseburia and Bifidobacterium ($p<0.001$). A negative correlation between the number of IV courses and gut diversity (Simpson's diversity index: correlation coefficient (r) = -0.383, $p=0.011$) and a positive correlation between FEV1 and gut diversity (Simpson's diversity index: $r= 0.47$, $p=0.0015$) occurred in those with CF.

This study highlights that patients with CF have an altered gut microbiota which correlates with clinical outcomes.

(Study Funding: European Commission for CFMATTERS Grant agreement no. 603038)

O: 6

Microalgal Omega 3 polyunsaturated fatty acids (PUFAs) effects on cognition, sociability, depressive-like behaviour and brain fatty acid composition in C57BL/6 mice

Submitting Author: Clara Seira-Oriach

List of Authors: Clara Seira-Oriach (b,a). Ruairi Robertsonc(a,e), R. Paul Ross (a,c), John F. Cryan (a,d),Catherine Stanton (a,c), Timothy G. Dinan (a, b)

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(b) Department of Psychiatry, University College Cork, Ireland
(c) Teagasc Food Research Centre, Moorepark, Fermoy, Cork
(d) Department of Anatomy and Neuroscience, University College Cork, Ireland
(e) School of Microbiology, University College Cork, Cork, Ireland

Discipline/Area: APC Microbiome Institute and Department of Psychiatry, University College Cork, Ireland

Abstract:
Essential omega 3 polyunsaturated fatty acids (n-3 PUFAs) play a critical role in brain development and function, especially during prenatal development and the early postnatal period. Using dietary interventions, we assessed the effects of n-3 PUFA supplementation or deficiency in pregnant mice on the behavioral phenotypes of offspring with cognitive, depressive-like and sociability tests. We later assessed the brain lipid composition in the adult offspring. Three separate cohorts of C57BL/6J female mice were fed with either control standard chow, n-3 PUFA deficient diet (absence of essential omega-3s) or n-3 PUFA enriched diet (1g EPA+ DHA/100g diet) from gestational day 0. Male offspring were weaned on to the same corresponding diets and behavioral tests were performed during both adolescence and adulthood. Moreover, long chain fatty acid analysis was subsequently carried out by gas-chromatography flame ionization detection on several brain regions of the adult offspring. n-3 PUFA enriched diet improved cognitive performance as shown by enhanced memory in the novel object recognition test during adulthood compared to the control group. In addition, this supplementation resulted in enhanced corticosterone recovery in response to acute stress (forced swim test - FST) in adolescent mice compared to both controls and the n-3 deficient group. n-3 PUFA deficient mice presented a depressive-like phenotype displayed by greater immobility during the FST compared to the control group. Moreover, n-3 PUFA deficient mice showed memory impairment in the novel object recognition test compared to the supplemented group in both adolescence and adulthood. In addition, n-3 PUFA deficient mice presented sociability impairments compared to both the control and n-3 enriched groups in adulthood. As compared with the control and deficient groups, mice on the n-3 PUFA enriched diet displayed a higher level of n-3 PUFA composition in several brain regions with concomitant decrease in n-6 PUFAs. These data suggest that perinatal dietary n-3 PUFA deficiency causes major impairments in cognitive, sociability and depressive-like behavior, while n-3 PUFA supplementation enhances longterm cognitive behavior and attenuates stress responsivity to an acute stress. These behavioral effects, which were more pronounced in adulthood than adolescence, may be related to increased n-3 PUFAs in the brain. Therefore, these findings show the importance of n-3 PUFA intake on brain development and indicate a potential role for these essential fatty acids in the etiology and treatment of psychiatric disorders.

All experiments were approved by the Animal Experimentation Ethics Committee of UCC. The authors are supported in part by Science Foundation Ireland in the form of a centre grant (APC Microbiome Institute grant number SFI/12/RC/2273); the Health Research Board of Ireland (Grant Numbers HRA_POR/2011/23 and HRA_POR/2012/32); the Sea Change Strategy, NutraMara programme (Grant-Aid Agreement No. MFFRI/07/01); and the SMART FOOD profect: 'Science Based 'Intelligent'/Functional and Medical Foods for Optimum Brain Health, Targeting Depression and Cognition' project (Ref No. 13/F/411) with the support of the Marine Institute and the Department of Agriculture, Food and the Marine (DAFM) in Ireland.

O: 7

Investigation into the role of autophagy in differentiation in leukaemia

Submitting Author: Dalyia Benjamin

List of Authors: Benjamin DB (1,2), O'Donovan TR(1), Orfali N, Mongan NP, Gudas LJ, Cahill MR (2), McKenna SL (1)

(1) Cork Cancer Research Centre, University College Cork
(2) CUH, Cork

Discipline/Area: Cork Cancer Research Centre, University College Cork and CUH, Cork

Abstract:
The term acute myeloid leukaemia (AML) describes a heterogeneous group of clonal disorders of hematopoietic progenitor cells, characterized by a failure in differentiation, leading to accumulation of immature blood cell precursors in the bone marrow and peripheral circulation. AML is the most common acute leukaemia in adults. Pharmacologic override of the cellular differentiation block in AML is an attractive strategy for intervention with a favourable toxicity profile. Success in 'differentiation therapy' has been achieved with the use of all-trans –retionic acid (ATRA) for the treatment of acute promyelocytic leukaemia (APL)1.

Autophagy has now been shown to play a key role in differentiation of blood cells (1). This work has identified several autophagy related genes that are up-regulated following differentiation of leukaemia cells. In this current project we are aiming to further investigate how these genes influence differentiation and autophagy. The impact of autophagy modulation with pharmacological agents is also being examined in AML patient samples obtained from Cork University Hospital. To assess differentiation and autophagy we are examining cell surface markers (CD11b, CD34) by flow cytometry, morphological features of differentiation, markers of autophagy (LC3I/II, GATE16) by Western Blot, autophagy assay-CytoID, and Colony Forming Unit assays to assess survival.

This project is intended to advance our understanding of differentiation and discover new avenues for therapeutic interventions in other AML subtypes.

1. Orfali N, O'Donovan TR, Nyhan MJ, Britschgi A, Tschan MP, Cahill MR, Mongan NP, Gudas LJ, McKenna SL. Exp Hematol. 2015; 43(9):781-793

O: 8

Sarcopenia, Myosteatosis & Weight loss: Negative Prognostic Indicators in Patients with Foregut Cancers

Submitting Author: Louise Daly

List of Authors: L Daly (1), S Cushen (1), E. Ni Bhuachalla (1), F Dwyer (1), P McEneaney (3) , S O'Reilly (2), DG Power (2), AM Ryan

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Discipline/Area: School of Food and Nutritional Sciences, University College Cork

Abstract:
Sarcopenia, myosteatosis (low mean skeletal muscle attenuation/density)(MA) and weight loss (WL) have been shown to significantly reduce survival in lung and GI cancer patients1. Little is known about the impact of sarcopenia and myosteatosis in foregut cancers.

A prospective study of patients with foregut cancers receiving chemotherapy. Malnutrition risk was assessed using the Malnutrition Universal Screening Tool, and Quality of life was assessed by EORTC QLQ-C30. Skeletal muscle cross-sectional area at L3 was measured by CT to diagnose sarcopenia and low MA using established cut offs1. Univariate and multivariate analyses for overall survival were conducted using the cox proportional hazards model; hazards ratios (HR) and corresponding 95% confidence intervals (CI) were obtained.

175 patients were included, 120 (69%) were male with a mean age of 64 years. In total 51% were overweight or obese and 7% underweight by WHO standards. 46% were sarcopenic. At censoring, 90 patients (51%) had died. Overall median survival was 16 months. Patients with low MA, sarcopenia and WL (>8%) had a median survival of 267 days vs 519 days in patients without these three conditions (p=0.001). On multivariate analysis, (controlling for age, sex, cancer type, ECOG, & treatment intent) patients exhibiting 3 conditions had a significantly increased mortality rate (HR 3.29, CI;1.5-7.1, p=0.003). WL (>8%) in the previous 6 months occurred in 71 patients (41%) and was significantly associated with lower physical and social function and higher symptom scales in particular appetite loss, fatigue, nausea and vomiting.

Regardless of overall body weight, the combination of low MA, sarcopenia and WL (>8%) independently predicts reduced survival in foregut cancers.

1. Martin L, Birdsell L, MacDonald N et al. J Clin Oncol. 2013; 12: 1539-1547.

Acknowledgements: This research was conducted with the financial support of Science Foundation Ireland (SFI) under Grant Number 07/CE/B1368

O: 9

The design and validation of a novel semiautomatic lung navigation platform

Submitting Author: Kashif Ali Khan

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Discipline/Area: Department of Respiratory Medicine, Cork University Hospital and School of Engineering, University College Cork

Abstract:
Introduction: In the era of lung cancer screening, tissue acquisition of peripheral lung lesions remains a challenge. We have developed a 3D electromagnetic navigation platform with airway segmentation and virtual bronchoscopy using a open source 3D slicer environment.

Methods: The open source visualisation software (3D Slicer www.slicer.org) created a detailed airway segmentation and virtual bronchoscopy model from acquired CT images. A magnetic field emitter board provides tracking of a semiautomatic locatable sensor probe (SALP) in the working channel of the bronchoscopewith always-on tip tracked sensor and can be steered both manually and automaticaly with joy stick, for accurate localization of peripheral lung lesion. An extensive ex-vivo evaluation was performed in a breathing lung model that was developed using inflatable plasticized pig lungs in a negative-pressure. Following this, in-vivo real time navigation in a live porcine model using a selection of novel radioopaque fiducials placed endobronchially into distal airways.

Results: After completion of a selection of experiments using the breathing pig lung model, fiducials were placed endobronchially in our live porcine model. Thereafter, CT images were used to create a virtual airway 3D segmentation model. After multiplaner re-construction, land mark based registration was performed to align the CT and anaesthetised porcine. Manual and automatic navigation with the bronchoscope containing the SALP was performed. The average navigation distance covered was 85.3mm. The navigational system accurately determined 84% of the navigation points within the airways.

Conclusion: Our navigational platform is inexpensive and open source and is the first to utilize SALP. In our model, there is good agreement between the position of the sensor probe during bronchoscopic navigation and as visualised in virtual bronchoscopy. Further work is being carried out to improve registration and accuracy of the navigational system before a pilot study in patients with peripheral lung nodules.

The project is funded by HRB – Health Research Board (HRA/POR 2012/31) - Ireland in collaboration with Harvard Medical School and University of Texas MD Anderson Cancer Centre USA.

O: 10

Mutations of the immunodominant epitopes lead to humoral immune escape of Hepatits C Virus

Submitting Author: Amruta S. Naik

List of Authors: Naik AS (1), Harty C (1), Palmer BA (1), Crosbie O (2), Kenny-Walsh E (2), Fanning LJ (1)

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(2) Department of Gastroenterology, Cork University Hospital, Cork, Ireland.

Discipline/Area: Department of Medicine, University College Cork

Abstract:
Mutations in the epitopes against which the neutralising antibodies were previously produced facilitate viral immune escape (1). Fractionation of virus into antibody (Ab) associated and an Ab free population, followed by analysis at the molecular signature level presents an opportunity to enhance our understanding of evolution of viral envelope proteins and humoral immune escape (2). The objective of the current study was to analyse hypervariable region 1 (HVR1) of glycoprotein of quasispecies in Ab associated and Ab free fractions from sera from chronically infected hepatitis C patients. Study A examined the prevalence of detectable levels of antibody associated virus in a panel of 16 unrelated serum samples. Study B involved the temporal mapping of the presence and absence of antibody associated virus in a genotype 4a chronically infected individual over 10 years. Briefly, Ab associated virus was purified using Ab spin TRAP columns. In study A, out of 16 samples used in this study; (n=3/8) genotype 1b, (n=3/3) genotype 1a, (n=2/3) and genotype 3a were positive for a 306 bp region encompassing HVR1 in AAV fraction. qRT-PCR results showed that antibody binding to homologous HCV reduces infectivity of sdHCV. This trend of reduced infectivity was evident across genotypes 1b and 3a. In study B, using 27 amino acid peptides from the predicted HVRI sequence of Ab associated and Ab free viral RNA, we demonstrated that differential peptide binding was associated with a single amino acid change. We provide direct evidence that natural humoral immune escape of HCV can occur within the HVR1.

This work was funded by Molecular Medicine Ireland as a part of the Clinical & Translational Research programme.

References:
1. Thimme, R.; Lohmann, V.; Weber, F. Antivir. Res. 2006: 69, 129–141.
2. Moreau, I., O'Sullivan, H., Murray, C., Levis, J., Crosbie, O., Kenny-Walsh, E., and Fanning, L . Virology Journal. 2008: 5, 103

O: 11

Hepatitis E Virus Infection in Ireland

Submitting Author: Caitriona Hickey

List of Authors: Hickey C (1), Spillane D (1), Benson J (1), Cryan B (1), O'Mullane J (2), O'Mahony S (3), Crosbie O (3), Levis J (4), Fanning L (4), Prentice MB (1,5)

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(3) Department of Gastroenterology, Cork University Hospital
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(5) Department of Microbiology, University College Cork.

Discipline/Area: Department of Microbiology, Cork University Hospital

Abstract:
Hepatitis E virus (HEV) is a single stranded RNA virus causing infection worldwide. Outbreaks are well recognised in developing countries where transmission between individuals is faecal-oral via contaminated water supplies, and are typically HEV genotypes 1 and 2. Recently, infections with HEV have been increasingly detected in Europe and North America in patients with no history of travel. These endogenously acquired infections are caused by genetically distinct viruses (genotypes 3 and 4) and are thought to be a food-borne pig-associated zoonosis. Most infections are asymptomatic but significant morbidity and chronic infection may occur in those with prior liver disease or immunosuppression (1). Internationally reported seroprevalence rates vary considerably and with the availability of improved diagnostics have increased in many regions. In order to determine the current prevalence in this region of Ireland we performed an age-stratified sex-matched study using anonymised serum samples submitted in 2015 for routine testing to the microbiology laboratory. We detected anti- HEV IgG in 16/198 (8%) individuals with the highest rate being found in the 40-59 year old age group (13%). This rate is higher than reported for the same region in 1995 (0.4%) using a previous generation assay on sera from antenatal patients (2). This study provides evidence of HEV circulation in our population and reinforces the need for ongoing clinical and laboratory surveillance for this underdiagnosed and often silent viral infection

1. Kamar N, Dalton HR, Abravanel F, Izopet J. Hepatitis E virus infection. Clinical microbiology reviews. 2014;27(1):116-38.
2. Lynch M, O'Flynn N, Cryan B, Hampl H, Opstelten R. Hepatitis E in Ireland. European journal of clinical microbiology & infectious diseases: official publication of the European Society of Clinical Microbiology. 1995;14(12):1109.

O: 12

Cord blood leptin and gains in body weight and fat mass during infancy

Submitting Author: Carol Ní Chaoimh

List of Authors: Ní Chaoimh C (1,2), Murray DM (2,3), Kenny LC (2,4), Irvine AD (5), Hourihane JO'B (3) and Kiely M (1,2)

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(2) The Irish Centre for Fetal and Neonatal Translational Research (INFANT), UCC
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(5)Department of Clinical Medicine, Trinity College Dublin, Ireland

Discipline/Area: Cork Centre for Vitamin D and Nutrition Research, School of Food and Nutritional Sciences, University College Cork

Abstract:
Low umbilical cord leptin concentrations may promote a fast growth trajectory in infancy and predispose to obesity. We aimed to determine associations between cord leptin and changes in weight and body composition during infancy.

Participants were from the Cork Baseline Birth Cohort Study (n = 2137). Cord and 2-year leptin were measured in 334 and 303 children, respectively. Weight was measured at birth, 2, 6, 12 and 24 months. Body composition was assessed using air displacement plethysmography at 2 days and 2 months. Associations between cord leptin and changes in weight standard deviation score (SDS) in the first 2 years and changes in fat mass index (FMI) [kg/m2] and fat free mass index (FFMI) [kg/m2] were explored.

Cord leptin was positively associated with weight SDS and FMI at birth and was inversely associated with changes in weight SDS over the first 2 years. There was an inverse association between cord leptin and increases in FMI between birth and 2 months. Those in the lowest quartile of cord leptin were more likely to be overweight/obese at 2 years. There was no association between cord and 2-year leptin concentrations. Two-year leptin concentrations were higher in children who were overweight/obese at 2 years.

These are the first data to show that associations between low cord leptin and faster weight gain in infancy are driven by greater increases in fat mass, at least in the early post-natal period.

This work was supported by the National Children's Research Centre. Ethical approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals, ref ECM 5 (9) 01/07/2008 and the study is registered with the United States National Institutes of Health Clinical Trials Registry (http://www.clinical trials.gov), ID: NCT01498965. The study was conducted according to the guidelines laid down in the Declaration of Helsinki

O: 13

Potential causes of hazardous drinking in teenagers

Authors: Eimear Murphy and Ian O'Sullivan, Colaiste Treasa, Kanturk, Co. Cork.
BT young scientist 2014 winners

Abstract:
Aim: To investigate the association between adolescent alcohol consumption and their parent's consumption pattern and attitudes towards alcohol use.

Methods: A cross-sectional survey was undertaken. Univariate/multivariate logistic regression and chi-square tests were used in our analysis.

Results: 47% of parents and 34.2% of adolescents were hazardous drinkers. Using multivariate logistic regression we discovered the main parental factors were (i) father's hazardous drinking, (ii) the father permitting his adolescent to drink alcohol on special occasions (iii) the mother allowing her adolescent to drink alcohol on special occasions.

Conclusion: We found that a liberal attitude to alcohol and increased levels of consumption by the parent are linked to hazardous adolescent drinking behaviour.

O: 14

Basehunter- a bacterial based DNA detection

Submitting Author: Donnchadh O'Sullivan

List of Authors: Donnchadh O'Sullivan, Aoife O'Brien Horgan, Amy Keane, Brandon Malone, Leanne O'Sullivan, Shama Chilakwad, Timothy O'Flynn, Dr. Paul Young, Prof. Tommie McCarthy

Discipline/Area: School of Biochemistry and Cell Biology, University College Cork.

Abstract:
Our project is a novel bacterial method of DNA detection. We have developed a customisable, linearised, double stranded plasmid with two sticky overhangs. When the sticky overhangs come into contact with a target sequence, the binding of the DNA sequence to the overhangs circularises the plasmid. The circularised plasmid is then transformed into competent E. coli cells. Bacterial growth of green fluorescent colonies indicates a positive result, therefore the complementary DNA target sequence was present. This system could act as a cheap alternative to both digital and real time PCR, as target DNA fragments are amplified in living cells without the use of a costly PCR machine. This system could potentially be used as a diagnostic or screening tool for viral and/or bacterial infection such as Human Papilloma Virus, Mycobacterium tuberculosis. By improving sensitivity and specificity this system could also be used for the detection of genetic mutations resulting in disease such as cystic fibrosis.

Notes:

Poster Presentations:
Main Foyer WGB – Western Gateway Building, UCC.

P= Poster Number

P	Author	Abstract Title
1	Aguilera, Mònica *et al.*	Linking TLRs activation by the microbiota with changes in sensory-related markers in IBS patients and rats
2	Allen, Andrew P. *et al.*	Stress and cognitive performance in dementia caregivers
3	Allen, Andrew P. *et al.*	Bifidobacterium Longum 1714 attenuates stress-induced behavioural and physiology changes and modulates brain activity and neurocognitive performance in healthy human volunteers
4	Arooj, Parniya *et al.*	A Prospective analysis of patients referred to Rapid Access Lung Clinic (RALC) with Hemoptysis
5	Barrett, Kevin *et al.*	Molecular characterisation of Adherent-invasive Escherichia coli (AIEC)-induced inflammasome responses in the pathophysiology of Crohn's disease
6	Brady, Noeleen *et al.*	Dementia and delirium are prevalent among older people in the Emergency Department and short screening tools are highly sensitive for both conditions
7	Brint, Elizabeth *et al.*	Fas, and its adaptor FADD, differentially regulate LPS-induced Inflammatory Responses.
8	Brint, Elizabeth *et al.*	Regulation of TLR10 expression in Intestinal Epithelial Cells and macrophages
9	Corcoran, Luke *et al.*	Prevalence of Dysglycaemia in a hospital-based oncology population
10	Cremin, Suzanne *et al.*	Changing frequencies of sexually transmitted infections in a Cork STI clinic
11	Crotty, Sean	The incidence and treatment of hypophosphataemia in dialysis patients in the ICU of CUH
12	Curran, Eileen *et al.*	The Impact of Birth by Caesarean Section on Attention-Deficit/Hyperactivity Disorder: A Sibling Control Study
13	Cushen, Samantha *et al.*	Impact of body composition parameters on clinical outcomes in patients with metastatic castrate-resistant prostate cancer treated with docetaxel
14	Cussotto, Sofia *et al.*	Elucidation of the Neuronal Circuitry Underlying the Antidepressant Effects of a Medication Used In Treatment-Resistant Depression
15	Dahly, Darren *et al.*	Maternal Predictors of Infant Body Composition.
16	Daly, Louise *et al.*	The prevalence of sarcopenia increases during ipilimumab treatment for metastatic melanoma; the impact of body composition parameters on treatment toxicity
17	Daly, Bart *et al.*	Piloting anticipatory care plans in CUH
18	Di Blasi, Zelda *et al.*	The Effects of Intranasal Oxytocin on Cardiovascular and Psychological Stress Response: A double blind placebo-controlled RCT
19	Di Blasi, Zelda *et al.*	The influence of the practitioner-patient relationship on pain perception: a placebo-controlled RCT
20	Dillon, Christina *et al.*	The relationship between alcohol consumption and hospital-treated self-harm presentations during public holidays

21	Dolan, Erin *et al.*	Characterisation of cognitive dysfunction in an α-synuclein model of Parkinson's disease
22	Ebere-Anaba, Ann *et al.*	An exploratory study of barriers and facilitators of a healthy lifestyle behaviour among pregnant African women in Cork.
23	Falvey, Chloe *et al.*	UBE2L6 regulates apoptosis and autophagy in oesophageal cancer cells
24	Farrell, Eric *et al.*	Defining Incidence and Risk Factors for Incidental Thyroid Carcinoma
25	Fernandes, Philana *et al.*	Development of an immunogenic therapy targeting Pancreatic Cancer
26	Fox, Siobhan *et al.*	Developing the "Irish Guidelines for Palliative care in people with Parkinson's disease and related Parkinsonian Syndromes
27	Fox, Siobhan *et al.*	Exploring the palliative care and support needs of people with Parkinson's disease and their carers
28	Garcia, Daniel *et al.*	The role of motor control and learning in objective measures of technical skill proficiency
29	Guo, Jianfeng *et al.*	Delivery of siRNA using Antibody-Targeted Cyclodextrin Nanoparticles: In Vitro Anti-Leukaemia Effects and In Vitro Pharmacokinetics
30	Hand, Collette *et al.*	Do Irish periodic paralysis patients have a common genetic origin?
31	Hannon, Evelyn *et al.*	Are we measuring modifiable risk factors in acute stroke patients
32	Hannon, Evelyn *et al.*	Reducing Door to Needle Times for Ischaemic Stroke in Cork University Hospital (CUH)
33	Hanrahan, Michael *et al.*	Appropriate Use of Elective Coronary Angiography in Patients attending Cork University Hospital with suspected Coronary Artery Disease
34	Harty, Ciara *et al.*	Hepatitis C Regulates the Expression of ATG5
35	Healy, Michael *et al.*	Assessment of autophagy inducers and differentially expressed genes as modulators of chemo-sensitivity in oesophageal cancer
36	Hegarty, Shane *et al.*	Smad-interacting protein 1 is a novel regulator of nigrostriatal pathway development, and a therapeutic target for Parkinson's disease
37	Hoban, Alan *et al.*	Regulation of Myelination in the Prefrontal Cortex by the Microbiota
38	Hong Ngai, Chin *et al.*	HSPA 5 as Biomarker for Early Diagnosis of Diabetic Nephropathy
39	Hueston, Cara M. *et al.*	Lentiviral overexpression of interleukin-1β in the hippocampus induces neurogenesis-associated cognitive deficits in adult male rats
40	Hunt, Eoin *et al.*	Detecting the microbiome of the asthmatic lung
41	Hyland, Niall *et al.*	Microbiota Regulation of Bladder Toll-like Receptor Expression in Male and Female Mice
42	Jamal, Mobin *et al.*	Clinical outcome in patients with functional neurological symptoms: A 4-year follow-up study
43	Keane, Jonathan *et al.*	Mouse Models of the Microbiome in Colorectal Cancer.
44	Kelleher, Emily *et al.*	Barriers and facilitators associated with attending community-based interventions among families of overweight and obese children
45	Kelly, John *et al.*	Transferring the Blues: Depression-Associated Gut Microbiota Induces Neurobehavioural Changes in the Rat

46	Kozareva, Danka *et al.*	TLX, a regulator of neurogenesis, is required for microglial in the adult mouse hippocampus
47	Lapthorne, Susan *et al.*	Identification of mucosal and systemic markers for categorisation of Asthmatic patient severity
48	Levone, Brunno Rocha *et al.*	Corticosterone differentially affects neural progenitor cells derived from specific areas of the longitudinal axis of the hippocampus
49	Lone, Mutahira *et al.*	Development of a cranial nerve animation to enhance dental student learning
50	Long, Sarah Louise *et al.*	Rational selection of Lactobacillus strains based on bile salt hydrolase activity
51	Luczynski, Pauline *et al.*	The microbiota shapes amygdala volume and dendritic morphology
52	McGrath, Keith *et al.*	A Multi-Disciplinary Quality Improvement Project Aimed at Reducing Avoidable Readmissions Through Improved Discharge Processes
53	McGrath, Paul *et al.*	Malignant Pleural Effusions: Current differential diagnosis, management and outcome
54	McHugh, Sheena *et al.*	Improving diabetes care in Ireland: a realist evaluation of the National Clinical Programme for Diabetes
55	Murphy, Carola *et al.*	Bacterial-mediated DNA delivery to tumour associated phagocytic cells
56	Murphy, Clodagh *et al.*	Experiences of the use of Biosimilar Medication in Inflammatory Bowel Disease
57	Murphy, Keelin *et al.*	Automated neonatal brain volumetric analysis in Down syndrome
58	Ní Bhuachalla, Éadaoin *et al.*	Changes in nutritional status after minimally invasive oesophagectomy (MIO) with an enhanced recovery after surgery (ERAS) programme & aggressive nutritional intervention.
59	Nor, Aiman *et al.*	Potential therapeutic gain in stereotactic radiosurgery of cerebral arteriovenous malformations by radiation dose enhancement with gold nanoparticles.
60	O'Leary, James *et al.*	The nuclear receptor TLX regulates motor, cognitive and anxiety-related behaviours during adolescence and adulthood
61	O'Flynn, AnneMarie *et al.*	The Association of Night-Time Systolic Blood Pressure with Ultrasound Markers of Subclinical cardiac and Vascular Damage
62	O'Callaghan, Peter Anthony *et al.*	Molecular Diversity in the Hepatitis C Virus
63	O'Connor, Cathal *et al.*	Calculating the Impact of Population-level Implementation of the LEAP Protocol to Prevent Peanut Allergy
64	O'Connor, Antoinette *et al.*	Detecting Diabetes Mellitus and Prediabetes in patients with acute stroke.
65	O'Connor, Antoinette *et al.*	Should the use of the Extended Myositis Antibody (EMA) panel be part of the routine work-up in suspected myositis?
66	O'Donovan, Tracey *et al.*	Enhanced Autophagy – an effective treatment for drug resistant cancers
67	O'Flynn, James *et al.*	Long, non-coding RNAs in breast cancer: analysis of lncRNA patient profiles to influence experimental design of a tethered RNA system
68	Ó'Léime, Ciarán S. *et al.*	IL-IB negatively impacts upon expression of both inflamattory and neurogensis - associated signalling molecules in hippocampal neural stem Cells in vitro

69	O'Regan , Niamh *et al.*	Screening for delirium with the Six-item Cognitive Impairment Test
70	O'Regan , Niamh *et al.*	Pre-delirium Features Predict Delirium Onset
71	O'Regan , Niamh *et al.*	Can the NICE delirium screening criteria detect delirium?
72	O'Reilly, Sinead *et al.*	The Role of Communication between Health Professionals and Patients as a Factor in Patient Complaints in Obstetrics- a Mixed Methods Review from an Irish Maternity Hospital
73	O'Shea, Emma *et al.*	Northern Ireland Audit of Dementia Care in Acute Hospitals
74	O'Sullivan, Donnchadh *et al.*	Basehunter- a bacterial based DNA detection
75	Palmer, Brendan *et al.*	The sound of silence: analysis of invariant and synonymous codon sites across the E1/E2 gene junction in Hepatitis C virus
76	Peoples, Aine *et al.*	Can gene sequencing identify additional genetic variants predicting for 5-Fluorouracil toxicity? - A cohort of Irish patients
77	Pyrz, Katarzyna *et al.*	Community-based approach to food allergy management. A case of a trans-disciplinary study in the UK and Ireland.
78	Ramlaul, Navneet *et al.*	An audit of Liver Biopsies performed at the Department of Hepatology, Cork University Hospital
79	Rettedal, Elizabeth *et al.*	Bacteria in Patient Tumours: What, Where & How?
80	Rettedal, Elizabeth *et al.*	Probiotic Bacterial Trafficking To Tumours In Cancer Patients
81	Ronan, Nicola *et al.*	The impact of CFTR modulation on CT Thoraces, circulating inflammatory mediators and sputum microbiome in a single centre cohort of patients with Cystic fibrosis with the G551D mutation
82	Ryan, Paul *et al.*	Assessment of existing lay-person knowledge on the role and use of an Automated External Defibrillator in amateur sports clubs.
83	Sabra, Zeina *et al.*	Inflammation and gut permeability: implications for health and disease.
84	Stanton, Mike *et al.*	Development of Tumour Therapy and Imaging Strategies Utilising Bacteria
85	Sullivan, Ashley *et al.*	A combination of cytokines and LPS increase pro-inflammatory chemokine expression primary bronchial epithelia cells
86	Sweeney-Landers, Siun *et al.*	Membrane sweep at term gestation in CUMH; a case-control study
87	Togher, Katie *et al.*	Examining the relationship between prenatal maternal stress and anxiety with gastrointestinal function in a population of nulliparous pregnant women
88	Walsh, Elaine *et al.*	PHARMS Study (Patient Held Active Record of Medication Status)
89	Walsh, Elaine *et al.*	Economic impact of medication error: a systematic review
90	Williamson, Rachel *et al.*	Analysis of the molecular and cellular mechanisms regulated by magnesium sulphate in an in vitro model of the human placenta
91	Casey, Eve and Hynes, Cathy	Sugar On Trial: A Comparative Study to Assess the Relative Sweetness of Beet and Cane Sugar and the Resultant Potential for Sugar Reduction

P: 1

Linking TLRs activation by the microbiota with changes in sensory-related markers in IBS patients and rats

Submitting Author: Mònica Aguilera

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Abstract:
Visceral pain is a hallmark of Irritable Bowel Syndrome (IBS). Alterations in microbiota composition and host-bacterial systems appear to contribute to its pathology. However, the exact mechanisms implicated are currently unknown (1,2,3).

We investigated the relationship between sensory markers and toll like receptors (TLRs) in an animal model and in colonic biopsies of IBS patients and healthy controls. Sprague Dawley rats were treated (5days) with the TLR4 agonist LPS or the TLR7 agonist Imiquimod. Rat colons and human biopsies were assayed for gene expression of sensory markers, TLRs, defensin-α5 and cytokines and rat colons were assessed for secretory-IgA levels. Human and animal studies were carried out with approval from the corresponding institutional ethics committee.

Biopsies of IBS patients showed a significant up-regulation in cannabinoid receptor 1 and 2 (CB1, 2), vanilloid receptor 1 (TRPV1), TLR2, TLR7 expression, and minor changes in TLR4, TLR5 and defensin-α5 compared to controls. All nociceptor markers positively correlated with TLR2 and TLR7. TLR4/7 stimulation, to mimic IBS-associated responses, induced alterations in cytokines and s-IgA levels. LPS activation induced the expression of CB1, CB2 and TRPV1, while Imiquimod down-regulated TRPV1 expression.

The data suggest that stimulation of specific TLRs is enough to alter the expression of nociceptive markers identified in IBS patients, pointing towards an active communication between the microbiota and the intestinal neuro-immune pathways. Thus, the data supports a link between the microbiota and alterations in intestinal nociceptive markers which may lead to visceral pain, indicative of a potential mechanism involved in IBS pathogenesis.

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P: 2

Stress and cognitive performance in dementia caregivers

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Abstract:
Introduction: Dementia caregiving is associated with heightened stress as well as increased anxiety and depression (1). There is also emerging evidence that the chronic stress of dementia caregiving may impact upon central nervous system activity in informal caregivers (2). The current study aimed to examine the cognitive neurobiology and mental well-being in dementia caregivers.

Methods: Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals. We also conducted a systematic review to gauge the currently known biological impact of family dementia caregiving. Caregivers and controls completed validated tests of stress, sleep quality, anxiety, and depression. Participants also completed cognitive tasks from the CANTAB battery assessing memory, attention and executive function. Stool, blood, urine, hair and saliva samples were collected from caregivers.

Results: Our systematic review indicates evidence of altered HPA axis activity and proinflammatory phenotype in caregivers. Our preliminary study results suggest the presence of higher levels of stress and depressive symptoms than controls. Caregivers also made a higher number of errors on the paired associates learning task (PAL), which engages the hippocampus, suggesting poorer visuospatial memory.

Conclusions: Dementia caregiving is associated a proinflammatory phenotype and high self-reported stress levels. This likely contributes to higher levels of depressive symptoms and may underpin a possible cognitive neurobiology of caregiving. A comprehensive physiological phenotyping of dementia caregivers is required to better understand the mechanisms of these effects.

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P: 3

Bifidobacterium Longum 1714 attenuates stress-induced behavioural and physiology changes and modulates brain activity and neurocognitive performance in healthy human volunteers

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Discipline/Area: Department of Psychiatry and Neurobehavioural Science/APC Microbiome Institute, University College Cork

Abstract:
Introduction: Precise targeting of the microbiome-gut-brain axis with psychobiotics - live microorganisms with a potential mental health benefit –is a novel approach for the management of stress-related conditions (1). Preclinical studies have identified B. longum 1714 as a putative psychobiotic with an impact on stress-related behaviours, physiology and cognitive performance (2,3). This study investigated whether these effects could be translated to human volunteers.

Methods: Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Healthy male volunteers (N = 22) ingested B. longum 1714 or placebo daily for four weeks each in a repeated-measures design. Participants completed study visits at baseline, post-placebo and post-probiotic. Acute stress was assessed using the socially evaluated cold pressor test, and daily stress was assessed via validated online questionnaires. Cognitive performance was assessed using the CANTAB platform and neurological activity via resting electroencephalography (EEG).

Results: In response to acute stress, B. longum 1714 led to a reduction in cortisol output and a blunted increase in subjective anxiety. Self-reported daily stress was lowered during daily psychobiotic consumption. There was a subtle improvement over placebo in visuospatial memory performance in paired associate learning (PAL) in the B. longum 1714 group. Fz mobility was higher following B. longum 1714 consumption compared to baseline and placebo.

Conclusions: B. longum 1714 is associated with attenuated responses to acute stress, a modest improvement in cognitive performance and altered resting EEG. Further studies are warranted to evaluate the benefits of this putative psychobiotic in relevant stress-related conditions.

P: 4

A Prospective analysis of patients referred to Rapid Access Lung Clinic (RALC) with Hemoptysis

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Abstract:
Background: After completing a retrospective analysis of all cases referred to our RALC with hemoptysis in 2011-2012 (a quarter had hemoptysis and only a sixth had lung cancer), a prospective study was commenced

Methodology: A prospective study was carried out on all patients referred to RALC with hemoptysis from 2013-July 2015. The objective of the study was to identify frequency of different causes of hemoptysis and the diagnostic yield of CT and standard bronchoscopy

Results All 153 patients were included (94males, 22 nonsmoker/77 ex-smokers/ 54 current smokers) The main causes of hemoptysis were bronchitis 46.9%, idiopathic 18.4%, Lung Cancer 17%, others 9.5%, bronchiectasis 8.2%. Furthermore, 23.5% (n=36) of patients presented with a single episode of hemoptysis, 41.8% (n=64) with non-persistent (<2 weeks) hemoptysis and 35.9% (n=55) with persistent (> 2 weeks) hemoptysis. Lung cancer patients were more likely to have persistent hemoptysis (p= 0.034). The specificity of CT scans for lung cancer was 100%, however 5 patients had false negative standard bronchoscopy with CT showing metastatic disease.

Conclusions: A sixth of patient presenting with hemoptysis had lung cancer and more than half of this population has persistent hemoptysis. There were no false negative CT scans for lung cancer.

Keywords: hemoptysis, etiology, lung cancer, bronchitis, unknown /no cause cause, RALC

P: 5

Molecular characterisation of Adherent-invasive Escherichia coli (AIEC)-induced inflammasome responses in the pathophysiology of Crohn's disease

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Abstract:
Crohn's Disease (CD) is a chronic inflammatory bowel disease with an increasing incidence worldwide. CD is a complex disorder involving dysregulated immune responses, genetic susceptibility and environmental factors. Certain groups of bacteria have been associated to CD including adherent-invasive Escherichia coli (AIEC), which is present in up to 40% of CD biopsies. AIEC are distinguished from other E. coli strains by their ability to invade epithelial cells and replicate within macrophages. This suggests that AIEC may play a significant role in the pathology of many CD cases. The inflammasome is a multi-protein complex composed by a Nod-like receptor (NLR), which senses environmental signals, including bacteria, resulting in the activation of caspase-1 leading to the subsequent maturation and secretion of the pro-inflammatory cytokines IL-1β/IL-18. The aim of this study is to investigate the interaction between AIEC and the inflammasome during inflammation and homeostasis. Interestingly chronic Inflammation, such as that seen with CD, has been characterised by high levels of expression of inflammatory cytokines such as IL-1β. Human intestinal epithelial cells infected with the AIEC strain HM605 showed increased expression of the inflammasome-associated genes Caspase 1, IL-1β, IL-18 and caspase 4 when compared to uninfected cells. Similarly we showed that caspase 1 expression is increased in AIEC-infected murine macrophages. Furthermore, colons of mice infected with HM605 and challenged with dextran sodium sulphate present an induction in IL-1β and IL-18 expression. Overall, our data suggest that AIEC-Inflammasome interactions may be playing role in the pathology of CD.

Acknowledgements: This research was conducted with the financial support of Science Foundation Ireland (SFI) under Grant Number SFI/12/RC/2273.

P: 6

Dementia and delirium are prevalent among older people in the Emergency Department and short screening tools are highly sensitive for both conditions

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Abstract:

Dementia and delirium are under-diagnosed in older hospitalised patients, the most vulnerable of whom are admitted via the Emergency Department (ED). ED staff need fast, valid tools to identify potential cognitive vulnerability in older attendees.

A trained researcher assessed ED attendees ≥70 years for dementia and delirium using the Mini Mental State Examination, Delirium Rating Scale–Revised 98 (DRS-R98; cut-off 18) and Informant Questionnaire on Cognitive Decline in the Elderly (cut-off 3.5). An expert later reviewed the data and assigned diagnoses. A second researcher blindly assessed patients, within 3-hours, using the 4-AT and Six-Item Cognitive Impairment Test (6-CIT).

Of 185 patients, 45.4% were female; median age 77 years (IQR 9); 24% had dementia and 16% delirium. There was significant concordance between DRS-R98 and 4-AT delirium categorisation (Cohen's Kappa 0.72; p<.001). Only 16 cases (9%) disagreed, with 4-AT falsely negative in three, positive in 11 cases with borderline/subsyndromal delirium, and two with no DRS-R98 defined delirium. Overall, 4-AT indicated possible delirium in 23%, with positive predictive value (PPV) 0.68 (CI 0.51-0.81) and negative predictive value (NPV) 0.98 (0.93-0.99; Area Under Curve (AUC) 0.95). The 6-CIT was abnormal in 32%, with PPV 0.49 (0.35-0.63) and NPV 0.89 (0.82-0.94) for dementia (pre-specified cut-off 9/10; AUC 0.74); and PPV 0.44 (0.31-0.59) and NPV 0.95 (0.90-0.98) for delirium (pre-specified cut-off 10/11; AUC 0.80).

This study demonstrates the potential of 6-CIT and 4-AT in ED to quickly and accurately exclude dementia and delirium. Specificity/positive predictive values for delirium are fair, but better for 4-AT than 6-CIT.

P: 7

Fas, and its adaptor FADD, differentially regulate LPS-induced Inflammatory Responses

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Abstract:
Recent studies have shown that the death-receptor Fas can also induce inflammatory responses. The aim of this study was to determine whether engagement of Fas could modify TLR4-induced inflammation.

Fas engagement on macrophages using an agonistic Fas antibody CH11, augmented LPS-induced NF-κB responses, causing an increase in the level of TNFα, IL-10, IL-8, IL-6 and IL-12. Conversely, co-stimulation of THP1s with both LPS and CH11 caused a significant reduction in the level of IFNβ production. This was also observed in immortalised murine bone marrow derived macrophages. This effect was seen to be dependent on the Fas adaptor FADD as LPS-induced IL-6 production was increased, whilst IFNβ production was suppressed, in $FADD^{-/-}$ murine embryonic fibroblasts. Overexpression studies utilising an IFNβ-luciferase promoter, an Interferon stimulated Regulatory Element (ISRE)-luciferase construct and an NFκB-luciferase construct have confirmed the differential effects of FADD on these pathways. Overexpression of the FADD-Death Domain (FADD-DD), inhibited LPS-induced ISRE and IFNβ but not NF-κB luciferase. Moreover, the FADD-DD was seen to inhibit TRIF- but not TRAF-3- or IKKε-induced ISRE-Luciferase, indicating that FADD may be exerting its effects at the level of TRIF. Overexpression of full-length FADD inhibited LPS-induced NF-κB-luciferase activation but was seen to augment LPS-induced IFNβ-luciferase.

In conclusion, these data show that activation of Fas and also its adaptor FADD have differential effects on the two arms of the TLR4 pathway. It is possible that engagement of Fas and availability of FADD may act as a regulatory switch to determine which pathway is activated.

P: 8

Regulation of TLR10 expression in Intestinal Epithelial Cells and macrophages

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Abstract:
Toll like receptors (TLRs) recognise pathogen associated molecular patterns and body's earliest responding sentinels to infection. 10 TLRs have been identified in humans with specific ligands now known for all TLRs, except TLR10. Recently it has been identified that TLR10 is a key player in the host response to infection, being essential for the induction of inflammation to both L. monocytogenes and Influenza (1, 2) in both macrophages and intestinal epithelial cells (IECs). In order to further characterise the role of this protein in host defense the aim of this project is to determine the regulation of TLR10 expression in both IECs and macrophages and also to characterise other eneteric infectious organisms detected by TLR10.

IEC lines were stimulated with a panel of ligands for TLRs 2, 4 and 5 and TLR10 expression examined. TLR10 expression was induced in the HT29 IEC line in response to FSL1 (TLR2/6 ligand) and to LTA (TLR2 ligand). In contrast, these ligands did not induce expression of TLR10 in either the HCT116 or the SW620 cell lines. In these cells only PAM3CSK4 (TLR1/2 ligand) was seen to induce TLR10 expression. In the THP1 monocyte cells, TLR10 expression was most potently induced in response to PAM3CSK4 and LPS. Furthermore, Infection of cell lines with the gram negative E.coli HM605 induced TLR10 expression. In conclusion TLR10 expression appears to be regulated by TLR2 and TLR4. We are currently investigating the effect of supressing TLR10 expression on immune response to HM605 infection.

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P: 9

Prevalence of Dysglycaemia in a hospital-based oncology population

Submitting Author: Luke Corcoran

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Discipline/Area: Final year Medicine student, University College Cork

Abstract:
Dysglycaemia is an abnormal blood sugar value. It is common in hospital-based patients, but data on its prevalence in oncology patients is generally lacking. This group has a number of risk factors for dysglycaemia including advancing age, malignancy, and treatment modalities (especially steroids). Dysglycaemia is associated with increased morbidity and mortality, so its identification and treatment should form an important aspect of care. Our project aims to answer the questions; what is the prevalence of dysglycaemia in an oncology day-ward population and who are those at greatest risk?

The 208 patients admitted to the Oncology day-ward in the Bons Secours hospital, cork were tested for evidence of Diabetic illness. This was done by the addition of two blood tests to their routine bloods, namely A blood glucose and HbA1c test. Any patients identified with potential diabetes were referred to the endocrinology team in the Bons. Demographic data, diabetes status, type of cancer, steroid use etc. was also recorded from the patient notes. The data was then entered into a computerised database for subsequent statistical analysis, with a view to estimating the prevalence of dysglycaemia and risk factors for same. The identification of patients was based on the WHO guidelines for the diagnosis of diabetes.

The Basic analysis has shown an prevalence rate of 28.4% (59/208). This is significantly higher than the prevalence rate of 6.5% in the general population.

This study has shown that there is an increased prevalence rate in oncology patient populations. It indicated the need for screening of patients to identify potential diabetic patients. We hope to create a risk stratification score for use on patients as part of standard care going forward.

P: 10

Changing frequencies of sexually transmitted infections in a Cork STI clinic

Submitting Author: Suzanne Cremin

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Abstract:
Epidemiological control of infection is essential to the sexual welfare of a community. It is therefore important to audit frequencies of sexually transmitted infections in order to inform clinical practice, to allow planning and allocation of resources and to help identify at-risk groups. We looked at the epidemiology of five common infections including anogenital warts, Chlamydia, Herpes Simplex, Neisseria gonorrhea and Syphilis. Information was collated from patient charts.

Details to follow.

P: 11

The incidence and treatment of hypophosphataemia in dialysis patients in the ICU of CUH

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Abstract:
Introduction: Hypophosphataemia is an almost inevitable complication in patients receiving dialysis (continuous renal replacement therapy "CRRT"). There is no consensus between physicians on the best treatment option and at what cut-off point should treatment be initiated.

Method: A retrospective audit was conducted of patients receiving CRRT during the calendar year of 2014 in the ICU of CUH. Analysis of each patients' phosphate levels throughout the entirety of their CRRT was noted and the administration of boluses or not and the level at which administered.

Results: Levels of hypophosphataemia were divided into mild, moderate and severe (<0.8, <0.5 and <0.3 respectively). Of the sample size (N=82), 43 experienced mild hypophosphataemia (52%), 14 moderate (17%) and 3 severe (0.04%). 22 boluses were administered at an average phosphate level of 0.58 (range 0.3 to 0.83). The mean increase in phosphate levels 6, 12 and 24 hours post administration was 0.15, 0.13 and 0.14 (SD 0.22) respectively. A group who fell to similar levels as the bolus group yet did not receive a bolus was identified. Their phosphate levels 6, 12 and 24 hours post their lowest reading were 0.10, 0.145 and 0.24 (SD 0.18) respectively.

Conclusion: The 52% incidence in this study depicts how commonly it occurs yet there are still huge discrepancies in the level at which supplementary boluses are given and the apparent poor efficacy of these boluses. Therapy practices for hypophosphataemia should thus be re-evaluated with a view of continuous phosphate infusions which show efficacy in international studies.

P: 12

The Impact of Birth by Caesarean Section on Attention-Deficit/Hyperactivity Disorder: A Sibling Control Study

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Discipline/Area: The Irish Centre for Fetal and Neonatal Translational Research (INFANT), Department of Obstetrics and Gynaecology, UCC

Abstract:
Background: It's possible that birth by Caesarean section (CS) may affect psychological development through early term birth or changes in microbiota or stress response. We assessed the impact of mode of delivery, specifically birth by Caesarean section (CS) on the development of attention-deficit/hyperactivity disorder (ADHD).

Methods: The study cohort consisted of all singleton live births in Sweden from 1990-2008 using data from Swedish national registers. Mode of delivery was defined as: unassisted vaginal delivery(VD), assisted VD, elective CS or emergency CS. ADHD was determined using International Classification of Diseases version 10(code F90 or F98.8), or prescription for ADHD medication. We used Cox regression to assess the association between birth by CS and ADHD in the total study population, adjusting for perinatal and socio-demographic factors. We then stratified analysis on maternal ID to assess the association amongst siblings.

Results: Our cohort consisted of 1,722,548 children, and 47,778 cases of ADHD. In the cohort analysis, the HR of the association between elective CS, compared to unassisted VD, and ADHD was 1.15[95% CI:1.11-1.20], but was attenuated among siblings(HR=1.05;[95%CI:0.93-1.18]). The HR of the association between emergency CS and ADHD was 1.16 in the cohort[95%CI:1.12-1.20] and 1.13 among siblings[95%CI:1.01-1.26].

Conclusion: Birth by CS is associated with a small increased risk of ADHD. However among siblings the association only remained for emergency CS. If this were a causal effect, the association would have also remained with elective CS, indicating this association is likely due to confounding.

Funding: The Irish Centre for Fetal and Neonatal Translational Research(INFANT) (Grant number 12|RC|2272).

P: 13

Impact of body composition parameters on clinical outcomes in patients with metastatic castrate-resistant prostate cancer treated with docetaxel

Submitting Author: Samantha Cushen

List of Authors: Cushen SJ (1), Power DG (2), Mc Dermott R (3), Daly L (1), MacEneaney P (4), O' Sullivan K (5), Aoife M Ryan (1)

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Discipline/Area: Food & Nutritional Sciences, UCC, Cork

Abstract:
Patients with loss of fat free mass (FFM) are prone to dose limiting toxicity (DLT) during chemotherapy. We examined the prognostic significance of body composition measurements, by computed tomography (CT), on chemotherapy toxicity and overall survival in patients with metastatic castrate resistant prostate cancer (mCRPC).

Patients with mCRPC, who were treated with docetaxel were included. Body composition parameters were measured at the third lumbar vertebra on CT images. Sarcopenia was defined using published cut-offs. Toxicity profile was assessed after 3 cycles of the drug and graded according to the National Cancer Institute Common Toxicity Criteria (version 4).

Overall 63 patients, mean age 69 years (SD 8.3), were included. Sarcopenia was present in 47% (n=30) and of these 26.7% (8/30) were sarcopenic obese. A DLT occurred in 22 (34.9%) patients. Neutropenia toxicity was significantly more frequent in sarcopenic patients than non-sarcopenic patients (15.4% vs. 0%, p=0.048). FFM (OR: 0.877, 95% CI: 0.780-0.985, p=0.027) was significantly associated with DLT. Visceral fat index (HR: 2.541, CI: 1.140-5.644, p=0.022) and anaemia (HR: 0.280, CI: 0.125-0.627, p=0.001) were predictive of reduced survival on multivariate analysis.

FFM is a significant predictor of DLT and visceral fat is associated with reduced survival in prostate cancer patients being treated with docetaxel chemotherapy. Sarcopenia is associated with increased haematological toxicity. Our results highlight the potential use of body composition measurements to predict clinical outcomes, such as toxicity and survival.

No funding to declare

P: 14

Elucidation of the Neuronal Circuitry Underlying the Antidepressant Effects of a Medication Used In Treatment-Resistant Depression

Submitting Author: Sofia Cussotto

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Discipline/Area: Department of Anatomy and Neuroscience, UCC, Cork

Abstract:
Approximately 50% of individuals with depression fail to achieve remission with first-line antidepressant treatment. Second-line treatment strategies for patients include dose optimization; switching to another antidepressant; combining antidepressants; or adding another type of drug to augment the effects of the antidepressant. One augmentation strategy is the addition of lithium to a tricyclic antidepressant. The neurobiological mechanisms underlying the therapeutic effects of lithium augmentation of antidepressants are currently unknown. Unravelling these mechanisms could aid drug development for treatment-resistant depression. The aim of this study was to identify brain areas that differentially respond to a combination of lithium plus antidepressant (desipramine) when compared to either treatment alone.

To this end, immunohistochemistry was used to measure drug-induced changes in ΔFosB/FosB expression (a marker of long-term neuronal activation) in the brain of a mouse strain that does not show antidepressant-like behavioural responses to desipramine or lithium alone, but that exhibits antidepressant-like responses to a combination of desipramine plus lithium. Mice received vehicle, lithium, desipramine, or lithium plus desipramine for 21 days, and ΔFosB/FosB-positive cells were counted in brain areas implicated in mood regulation.

In contrast to desipramine or lithium alone, a combination of lithium plus desipramine increased ΔFosB/FosB-positive cell density in the dentate gyrus and CA3 regions of the dorsal hippocampus. Differential drug effects were not observed in the medial prefrontal cortex, nucleus accumbens, amygdala or the hypothalamus. These data suggest that the dentate gyrus and CA3 regions of the dorsal hippocampus are key players in the neural circuitry underlying an effective antidepressant response.

P: 15

Maternal Predictors of Infant Body Composition

Submitting Author: Darren Dahly

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(2) Clinical Research Facility Cork, UCC, Cork
(3) The Irish Centre for Fetal and Neonatal Translational Research (INFANT), Cork University Maternity Hospital, UCC, Cork.

Discipline/Area: Department of Epidemiology and Public Health, University College Cork

Abstract:
The chances that a person becomes obese or develops diabetes can be influenced during their fetal development (1) in ways that are likely mediated by their body composition at birth (2). A better understanding of how maternal lifestyle is related to newborn body composition could thus inform intervention efforts (3).

Using Cork participant data from the *Screening for Pregnancy Endpoints* (SCOPE) cohort study (ECM5(10)05/02/08), we explored how maternal body size, gestational weight gain, exercise, alcohol, smoking, and diet were related to infant fat and fat-free mass. Maternal factors were measured by a trained research midwife at 15 gestational weeks. Infant body composition was measured using air-displacement plethysmography. Quantile regression (4) was used to relate maternal factors to infant outcomes.

Excess (versus healthy) gestational weight gain was associated with increased median fat-free mass (112g, 95%CI: 47 to 176) and fat mass (33g, 95%CI: 1 to 65) in the offspring. The apparent impact on the latter was amplified at the upper end of it distribution (103g increase in the 95th centile, 95%CI: 33 to 174). Maternal obesity (versus normal weight) was associated with increased median fat mass (48g, 95%CI: 12 to 84). The highest centiles of fat mass were lower among infants of women who engaged in frequent moderate-intensity exercise early in the pregnancy (-92g at the 95th centile, 95%CI: -168 to -16). No other lifestyle factors were strongly related to infant outcomes. These results suggest that supporting healthy maternal lifestyles can have a beneficial impact on infant body composition.

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This research was possible with funding from the Health Research Board (Interdisciplinary Capacity Enhancement award ICE/2012/12); The Cork BASELINE Birth Cohort Study is funded by the National Children's Research Centre, Dublin, Ireland. SCOPE Ireland is funded by the Health Research Board of Ireland (CSA/2007/2)

P: 16

The prevalence of sarcopenia increases during ipilimumab treatment for metastatic melanoma; the impact of body composition parameters on treatment toxicity

Submitting Author: Louise Daly

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Discipline/Area: Nutritional Science, University College Cork, Cork

Abstract:
Body composition is an important predictor of chemotherapeutic drug toxicity. Ipilimumab (ipi), a monoclonal antibody used to treat metastatic melanoma (MM) can result in immune-related adverse events (IRAE). No validated predictive biomarkers of Ipi toxicity exist & its impact on body composition has not been established.

Patients (pts) with MM, treated with Ipi between 2009-2015 were included. Skeletal muscle cross-sectional area at L3 was measured by CT at baseline and after 4 cycles of Ipi (12 weeks). Sarcopenia was defined using sex specific published cut-offs[(1)]. Toxicity was recorded (CTCAE V4.0).

81 pts (48 male), mean age 55 years were included. Overall 69% were overweight or obese & 36% were sarcopenic at baseline. No difference in the prevalence of GI, dermatologic, or endocrine IRAEs between sarcopenic and non-sarcopenic pts. Sarcopenic patients were more susceptible to early treatment cessation (38% vs 19 %, p=NS). Longitudinal changes in body composition (n=55) showed the prevalence of sarcopenia increased from 31% to 51% by completion of Ipi (p=0.004). Significant reductions were observed in skeletal muscle area, fat free mass, and fat mass after 4 cycles of ipi (151±38 vs. 145±38cm^2, p=0.003; 51.2±11.3 vs. 49.4 ± 11.3kg, p=0.003; 24.4±6.5 vs. 23.1 ± 7.0 kg, p=0.003 respectively). Overall 40% of pts experienced a meaningful muscle loss of >6cm^2 (equivalent to 1kg of skeletal muscle & associated with physical function).

MM pts with sarcopenic do not experience more toxicity but tend to spend less time on treatment. MM pts experienced a significant and rapid loss of muscle during treatment and should be encouraged toward isometric exercise and nutritional intervention in hope of retaining muscle mass.

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Acknowledgements: This research was conducted with the financial support of Science Foundation Ireland (SFI) under Grant Number 07/CE/B1368

P: 17

Piloting anticipatory care plans in CUH

Submitting Author: Bart Daly

List of Authors: Daly B, Healy L, Gallagher P, O'Connor M.

Discipline/Area: Department of Geriatrics, UCC and CUH, Cork

Abstract:
Introduction: Anticipatory care plans are documents designed to act as a guide to the level of care appropriate for individual patients. They are proven to improve patient care and providing better value for health services in NHS studies. Figures from Scotland, where such programs are widespread, indicate 10% of all patients will die during their current hospital admission. As EWTD regulations are implemented patients may be attended by their medical team just 24% of the time with the remainder being under the responsibility of on call physicians.

Aim:
i) Focus the patient's primary team to consider treatment goals
ii) Involve the patient and family in clarifying goals
iii) Provide guidance to staff unfamiliar with the patient as to appropriate care pathways

Methods: This project involves piloting of an anticipatory care plan for patients on a 36 bed elderly care/general medical ward in Cork University Hospital. The form has been designed in conjunction with leading physicians in elderly care medicine and palliative care. Stakeholders will be surveyed as part of this project and if successful the document will be implemented on a hospital wide basis.

Results obtained: A survey of medical registrars (95% response rate) showed all surveyed felt they had managed patients more aggressively than they felt ideal whilst on call in CUH.

Conclusion: Appropriate management of deteriorating patients can pose problems for medical registrars in CUH. Anticipatory care plans have previously been shown to improve patient care and guide appropriate management.

P: 18

The Effects of Intranasal Oxytocin on Cardiovascular and Psychological Stress Response: A double blind placebo-controlled RCT.

Submitting Author: Zelda Di Blasi

List of Authors: Zelda Di Blasi, Sinéad Forde, Janelle Logan Lane, Mike Murphy

Discipline/Area: School of Psychology, University College Cork

Abstract:
The stress-attenuating effects of oxytocin are well documented and there is some evidence that intranasal oxytocin can attenuate cortisol response in laboratory tasks, especially in clinical populations. Recently, a number of commercial intranasal
Oxytocin products have appeared on the market (e.g. *Oxytrust, Oxyluv)*, but there is little empirical research on the efficacy of these products.

We conducted a double-blind randomized control trial with 37 healthy volunteer college students who received either 20 IUs of Oxytocin spray (n=19, 11 females) or placebo spray (n=18, 9 females). Stress was induced via the Trier Social
Stress Test (TSST). Cardiovascular reactivity and recovery were monitored using Blood Pressure and Heart Rate. Anxiety and affectivity were assessed using the Positive and Negative Affect Scale (PANAS) and the State Trait Anxiety Inventory
(STAI) pre- and post-stress exposure.

There was no significant difference between Oxytocin and placebo spray and cardiovascular reactivity and recovery. Females who received Oxytocin had a decrease in negative affect, while males had a significant increase in negative affect.

Intranasal oxytocin was as effective as placebo in reducing reactivity during a stress task, among our group of healthy participants. We found sex differences in the emotional response to stress tests as identified previously in the literature.

P: 19

The influence of the practitioner-patient relationship on pain perception: a placebo-controlled RCT

Submitting Author: Zelda Di Blasi

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Discipline/Area: School of Psychology, University College Cork

Abstract:
There is extant research on the influence of pain management interventions, however much less is known about the effects of different forms of health care interactions on pain perception.

In this study, the effect of two styles of health care interaction on pain was evaluated on a randomised, single-blind, placebo-controlled study of 100 healthy volunteers. Fifty participants were randomised to receive an 'enhanced' interaction (e.g. friendly, reassuring) and 50 to receive a 'limited' interaction (e.g. neutral, formal, slightly rushed) on pain threshold and pain tolerance.

Participants were told that the aim of this study was to examine the effects of intranasal oxytocin on pain perception, and that they would receive either oxytocin or placebo spray. All participants were randomised to placebo. Measures included the Consultation and Relational Empathy Scale (CARE), the Credibility/ Treatment Expectancy Questionnaire, and the Cold Pressor Test (CPT).

Participants who were randomised to the enhanced consultation had significantly lower pain threshold than those randomised to the
Limited consultation (p=.29). Those participants also had significantly higher CARE scores.
In a laboratory setting, when participants perceive the research clinician as caring and empathetic, their pain response changes.

P: 20

The relationship between alcohol consumption and hospital-treated self-harm presentations during public holidays

Submitting Author: Christina Dillon

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(1) National Suicide Research Foundation Ireland
(2) Department of Epidemiology and Public Health, University College Cork, Cork

Discipline/Area: National Suicide Research Foundation Ireland

Abstract
Self-harm constitutes a significant public health problem. Alcohol consumption is frequently involved in cases of self-harm and is a common feature of public holidays. Evidence to support the relationship between alcohol consumption and self-harm during public holidays is limited[1].

Data on self-harm presentations to all emergency departments from 2007-2013 were obtained from the National Self-Harm Registry Ireland. Descriptive and logistic regression analyses were used to explore the relationship between alcohol consumption and self-harm presentations on public holidays compared to all other days in the year.

Between 2007 and 2013, the mean number of self-harm presentations was 32 (±7) daily and 36 (±11) on public holidays. New Year's Day and St. Patrick's Day showed the highest increases in mean self-harm presentations compared to all other public holidays, 42 and 56 respectively.

Self-harm presentations to hospital on a public holiday were 28% more likely to involve alcohol consumption compared to presentations on other days (OR: 1.28, $p<0.001$). Alcohol was involved in 42% of all self-harm presentations on bank holidays compared to 38% on all other days. Alcohol consumption was higher among males (44%) than females (39%).

The findings from this study show that alcohol consumption is associated with the higher rate of self-harm presentations on public holidays. National Strategies to reduce access to alcohol and increase awareness of risks associated with the use and misuse of alcohol should be intensified.

The National Suicide Research Foundation is funded by the HSE National Office for Suicide Prevention.

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P: 21

Characterisation of cognitive dysfunction in an α-synuclein model of Parkinson's disease

Submitting Author: Erin Dolan

List of Authors: Dolan EK, Nolan YM and Sullivan AM.

Discipline/Area: Department of Anatomy and Neuroscience, University College Cork

Abstract:
Viral vector-mediated-overexpression of α-synuclein in rodent brains in vivo is a newly-developed model of Parkinson's disease (PD). It reproduces many of the clinical features of PD, including dopaminergic-neuron degeneration in the substantia nigra (SN), decreased striatal dopamine levels and significant motor impairment. In addition to the characteristic motor symptoms of PD, cognitive dysfunction such as depression, dementia and dysexecutive syndrome can manifest as the disease progresses. Our study aims to investigate and characterise late-stage cognitive dysfunction using the α-synuclein rodent model. Adult male Sprague-Dawley rats received into the SN unilateral ($3.1x10^8$gc/3µl) or bilateral (2 injections of $1.6x10^8$gc/3µl) injection of AAV vector serotype 2/6 overexpressing human wildtype α-synuclein (n=10) or GFP (n=8). An additional cohort of control animals remained intact controls (n=8). Animals underwent various motor and cognitive tests at set time-points throughout the experiment. Immunohistochemical staining showed widespread transgene expression in the SN at 20 weeks post-surgery, with strong expression in the hippocampus, colliculi and septohippocampal nucleus at 40 weeks post-surgery. α-synuclein-injected animals exhibited significant motor dysfunction in the stepping test, first evident at 20 weeks post-surgery ($p<0.001$). Olfactory function, measured by an olfactory discrimination task, showed a trend towards significant impairment in the α-synuclein groups ($p=0.052$). There were no deficits in the conditioned taste aversion protocol. Interestingly, there were no differences between groups in spontaneous alternations, despite the presence of α-synuclein in the hippocampus. These results indicate that α-synuclein can accumulate throughout the brain following AAV-mediated-expression in the SN, and may play a critical role in PD-related cognitive dysfunction.

This work is supported by a grant from Molecular Medicine Ireland. All experiments were conducted in accordance with the European Directive 2010/63/EU, and under an authorization issued by the Health Products Regulatory Authority Ireland and approved by the Animal Ethics Committee of University College Cork

P: 22

An exploratory study of barriers and facilitators of a healthy lifestyle behaviour among pregnant African women in Cork

Submitting Author: Ann Ebere Anaba

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Discipline/Area: Departments of Epidemiology and Public Health, University College Cork

Abstract:
There is a lack of research conducted among the ethnic minority groups in Ireland, to particularly understand the unique role of factors such as religion, culture and communication, which may challenge healthy lifestyle behavior during pregnancy. Different studies and data have highlighted the trends and various types of mortality and morbidity associated with an unhealthy lifestyle in women during pregnancy and newborn (Michael Turner & Richard Layte 2013).

However, there are also cultural factors that may influence obesity including the preference for overweight, curvy women in the African community and indulging in cultural practices. For example, consumption of traditional foods high in fat is a recorded dietary and cultural practice in this ethnic minority group. (Airhihenbuwa C.O et al., 1996, Birtwum et al., 2005, Benkeser R.M 2012,).

Eight individual semi-structured interviews, using open-ended questions, a theoretical domain framework was used to identify the barriers and facilitators to a healthy lifestyle and also the influences of the behaviors on the African pregnant women.

The majority of participants perceived knowledge, emotion and environmental context as the main barrier to healthy lifestyle behavior during pregnancy. Most participants reported, not receiving any specific advice on physical activity and diet. Future research should focus on identifying the nutritional contents in African diet to equip the dieticians dealing with the ethnic minorities. Health-care providers should be more proactive in communicating the health benefits of a healthy lifestyle behavior during pregnancy to every pregnant woman.

This study is not funded, is a thesis submitted in partial fulfilment for the degree of Masters of Public Health 2015.

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3. Michael Turner and Richard Layte (2013).

P: 23

UBE2L6 regulates apoptosis and autophagy in oesophageal cancer cells

Submitting Author: Chloe Falvey

List of Authors: Chloe Falvey (1), Tracey O'Donovan (1), Michelle Nyhan (1), Seamus O'Reilly (2), Sharon McKenna (1)

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Discipline/Area: Cork Cancer Research Centre, Biosciences Institute, University College Cork

Abstract:
Oesophageal cancer incidence is rapidly increasing with thousands of new cases diagnosed every year. This remains one of the most difficult to treat cancers due to late stage presentation with drug resistant disease. In order to overcome this resistance, it is crucial that we understand the molecular mechanisms underpinning chemosensitivity of oesophageal cancer.

Affymetrix gene array analysis was used to identify genes which are differentially expressed between drug sensitive (OE21 and OE33) and drug resistant (KYSE450 and OE19) oesophageal cancer cells. Members of the ISG15 pathway were upregulated in drug sensitive cells and UBE2L6 was selected for functional analysis. The UBE2L6 gene was knocked down in OE21 cells by siRNA and effects on chemosensitivity were established by colony formation assay. Biochemical apoptotic markers were analysed by flow cytometry (active caspase-3, Annexin-V and mitochondrial depolarisation). Effects of knockdown on autophagy were established by examination of cellular morphology, flow cytometry (CytoID) and evaluation of LC3II by both western blotting and immunofluorescence.

Knockdown of UBE2L6 led to increased apoptosis and sensitivity to 5-FU. Significant autophagy induction was also observed. Furthermore, UBE2L6 significantly enhanced induction of autophagy by several known autophagy inducers (including valproic acid, rapamycin and Lithium). Autophagic flux was not disrupted. Knockdown of ISG15 did not affect chemosensitivity but was sufficient to promote autophagy.

Our data identifies a novel role for UBE2L6 in chemosensitivity. We have also characterised UBE2L6 as a regulator of autophagy and suggest that the ISG15 conjugation pathway is mechanistically important for this effect.

Funding: UCC SRF PhD Programme

P: 24

Defining Incidence and Risk Factors for Incidental Thyroid Carcinoma

Submitting Author: Eric Farrell

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(3) Endocrinology, SIVUH
(4) Otolaryngology SIVUH

Discipline/Area: Department of Medicine, University College Cork

Abstract:
Introduction: Thyroid cancer has shown one of the fastest growths in incidence of any cancer (1). An increasing proportion of thyroid cancers are incidentally discovered. Lymphocytic thyroiditis has recently been shown to be a risk factor for thyroid cancer in general. The objective of our study was to investigate the incidence of Incidental Thyroid Carcinomas (ITC) at our institution, and to investigate impact of lymphocytic thyroiditis and other risk factors on risk of ITC.

Methods: Retrospective review of 713 consecutive thyroidectomies. Cases with history or preoperative diagnosis of thyroid cancer, or with non-incidental cancer found in the index nodule constituting indication for surgery, were excluded. ITC was diagnosed as unexpected cancer occurring outside the index nodule. Lymphocytic thyroiditis was classified as absent, mild, or moderate/severe.

Results: 65 cases were excluded due to history or preoperative diagnosis of thyroid cancer, and 68 due to non-incidental cancer within the index nodule. Among the remaining 580 cases, there were 43 (7.4%) ITCs. ITCs were significantly associated with moderate/severe lymphocytic thyroiditis (MSLT) (relative risk 2.5, p=0.03) and complete (versus partial) embedding of the specimen (relative risk 3.3, p=0.001). Any lymphocytic thyroiditis, extent of surgery (total versus partial thyroidectomy), and TSH levels were not significant. Both MSLT and complete embedding remained significant on multivariate analysis.

Conclusions: Our data demonstrates a significant correlation between moderate/severe lymphocytic thyroiditis and incidental thyroid carcinoma. There was also an increased risk of ITC when all of the specimen was embedded for pathological examination as opposed to partial. In our study, patients with Grave's disease and moderate/severe lymphocytic thyroiditis were less likely to have ITC than those without Graves' disease and moderate/severe lymphocytic thyroiditis, this is in line with findings from other studies(2).

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P: 25

Development of an immunogenic therapy targeting Pancreatic Cancer

Submitting Author: Philana Fernandes

List of Authors: Fernandes P, O'Donovan TR, McKenna SL, Soden DM, Forde PF.

Discipline/Area: Cork Cancer Research Centre, University College Cork, Republic of Ireland.

Abstract:
Introduction: Pancreatic cancer is one of the deadliest cancers with 5-year survival only 3% (1). The majority of cases are surgically unresectable and show marked resistance to conventional forms of chemotherapy. Even with complete surgical resection, recurrence is common often confounded with distant metastases (2). Electroporation is a physical technology that renders the cell membrane permeable to otherwise poorly permeant chemotherapies (7). Electrochemotherapy has been shown to be effective at local tumour resolution with limited side effects (3). Additionally, preliminary studies have shown that ECT results in immune recruitment to the treated tumour but also reduces distal metastasis in murine models, allowing for extended survival (4-5).

Methods: Electroporation – Pancreatic cancer cells were resuspended in PI-containing electroporation buffer and electroporated at 0.4-1kV/cm in 4mm cuvettes (8 pulses of 99µs at a frequency of 1Hz) using a BTX electroporator. FACs – Cells were examined for fluorescence emission. Median fluorescence was determined and uptake calculated as a percentage relative to untreated cells. Morphology- Cells were cytospun, stained and visualised. C.F.A. – Cell recovery was assessed by standard clonogenic assay.

Results: Electroporation significantly increases PI-uptake by pancreatic cancer cells without effecting viability. Electroporation leads to transient morphological changes including the apparent disintegration of the plasma membrane and the presence of cytoplasmic vacuoles. Electroporation does not affect the ability of cells to recover and proliferate.

Conclusion: Electroporation has the potential to increase the uptake of chemotherapeutic drugs in pancreatic cancer cells thus potentiating any cytotoxic effect. Furthermore, electroporation induces transient morphological changes that may improve the immunogenicity of cell death.

Funding: The authors wish to acknowledge funding from the Pancreatic Cancer Research Fund UK and Breakthrough Cancer Research.

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5. Roux S, Bernat C, Al-Sakere B, et al. Cancer Immunology Immunotherapy 2008:57:1291-130

P: 26

Developing the "Irish Guidelines for Palliative care in people with Parkinson's disease and related Parkinsonian Syndromes

Submitting Author: Siobhan Fox

List of Authors: Fox S (1), Cashel A (2), Kernohan G (3), Lynch M (4), McGlade C (1), O'Brien T (5), O'Sullivan S (6), Timmons S (1)

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(2) Parkinson's Association of Ireland
(3) Institute of Nursing and Health Research, University of Ulster
(4) Irish Hospice Foundation
(5) Marymount University Hospital and Hospice
(6) Cork University Hospital

Discipline/Area: Centre for Gerontology and Rehabilitation, University College Cork

Abstract:
Introduction: Palliative care is recommended in all life-threatening illnesses. Research from across the island of Ireland shows that despite these recommendations, healthcare workers are unsure of the appropriateness of palliative care in their patients with Parkinson's disease (PD). Guidelines are recommended to improve referrals, and to encourage an integrated care approach. However, there were no previous guidelines for the palliative care of people with Parkinson's disease. The aim of this poster is to outline the process where we developed Irish Guidelines for Palliative care in people with PD and related Parkinsonian Syndromes.

Method: The process followed rigorous guideline development standards, as outlined by the Irish National Clinical Effectiveness Committee. An international advisory group of PD and palliative care experts was assembled to oversee the process, representing all of the key stakeholders. A systematic review to uncover previous guidelines was undertaken, and identified guidelines were adapted for the Irish context. A second systematic review of both drug and non-drug interventions in Parkinson's was conducted to inform the symptom management section of the guidelines.

Results: The key topics in the final guidelines included: Palliative care approach in PD; Communication and advance Care Planning; Multidisciplinary care; Physical care; Psychological care; Social care; Spiritual care; End-of-life care; Carers; Legal issues.

Conclusion: It is hoped that the learning from this guideline development process will encourage other groups to develop guidelines for palliative care in other neurological illnesses.

Funding: Grant received from Irish Hospice Foundation

P: 27

Exploring the palliative care and support needs of people with Parkinson's disease and their carers

Submitting Author: Siobhan Fox

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Discipline/Area: Centre for Gerontology and Rehabilitation, University College Cork

Abstract:
Introduction: Palliative care is recommended for non-malignant illnesses, including Parkinson's disease (PD). However, referral rates to specialist palliative care (SPC) are low, and research with healthcare workers in Ireland and the UK highlight unmet palliative needs in this population. However less is known about the views of people with PD and their carers about palliative care.

Method: Semi-structured interviews were conducted with people with PD (n=19) and carers (n=11). Interviews were transcribed, and analysed using Thematic Analysis. Ethical approval was received from the Cork Research Ethics Committee.

Results: People with PD and their carers are unfamiliar with the term palliative care; a 'fear' was not evident in these interviews. When informed of the role of palliative care, most felt that they would benefit from this input. Patients and carers experienced a high illness burden, and wanted extra support. Crisis times requiring SPC involvement may include at diagnosis, and advancing illness. Participants wanted more information about palliative care, and especially further supports to address their psychosocial needs.

Conclusions: The holistic and person-centered approach of palliative care can address the complex physical and psychosocial symptoms experienced by people with PD and their carers. A generalist palliative care approach should be adopted by all healthcare workers, with most palliative care needs responded to within existing disease management programmes, and SPC responding where needed. Further education about palliative care services among people with PD and their carers is essential so that they can access these services as needed.

Funding: Grant received from Irish Hospice Foundation

P: 28

The role of motor control and learning in objective measures of technical skill proficiency

Submitting Author: Daniel Garcia

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Discipline/Area: Department of Medicine, University College Cork and Department of Kinesiology, McMaster University, Hamilton, Canada

Abstract:
Computerized technologies in precision clinical skills assessment can provide objective information about a practitioner's efficiency (e.g., fewer number of movements made to complete a task infer increased efficiency (1)). Further, how an educator chooses to define the beginning and end of each movement can impact the nature of these measurements. To illustrate this, we validated the Imperial College Surgical Assessment Device (ICSAD) by comparing it to a high resolution VICON motion-tracking system. Sensors from both systems were fixed to a manipulandum and moved along a sliding track 20 times, comparing the number of movement calculated by each device. Given the reduced resolution of the ICSAD, we hypothesized that the lower, default velocity threshold would provide significantly greater errors in movement count than a more conservative threshold. The hypothesis was tested in a 2 Device (ICSAD, VICON) by 2 Velocity Threshold (7.4mm/s, 15mm/s) ANOVA on movement errors calculated (|20 – number of movements|). The analysis supports our hypothesis, revealing the ICSAD provides significantly more inaccurate movements measured when compared to VICON at the default velocity threshold. That is not to say that the ICSAD is an inadequate tool. When set properly, the ICSAD is as effective as the more resolute VICON system. The integration of objective computerized measures requires a specialized understanding of modern motor control and learning to ensure accurate results are obtained from assessments and errors are avoided. This research helps us understand how objective motion-capture systems may be used to improve methods of competency assessment in technical skill education.

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P: 29

Delivery of siRNA using Antibody-Targeted Cyclodextrin Nanoparticles: In Vitro Anti-Leukaemia Effects and In Vitro Pharmacokinetics

Submitting Author: Jianfeng Guo

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Discipline/Area: School of Pharmacy, University College Cork

Abstract:
Background and Aims: Delivery of small interfering RNA (siRNA) using multifunctional nanoparticles has been investigated to treat solid cancers; however, the application of this approach to blood cancers is at an early stage. An antibody-targeted cyclodextrin-based nanoparticle (NP) has successfully been engineered to specifically deliver siRNA to acute myeloid leukaemia (AML) cells via CD123 antigen [overexpressed on AML cells and leukaemia stem cells (LSCs)] [1]. Our previous results show specific banding of antibody-targeted cyclodextrin NPs incorporating Bromodomain-containing protein 4 (BRD4) siRNA to KG1 cells (an AML cell line) and AML cells in blood from previously untreated patients resulting in gene knockdown and anti-proliferation [1]. The aims of this study are; to investigate the anti-leukaemia effects of this NP *in vitro* using KG1 cells and to evaluate pharmacokinetics (PK) of the NP in mice.
Methods: The antibody-targeted cyclodextrin NP was prepared as previously described [1]. Briefly, the amphiphilic cationic cyclodextrin was complexed with siRNA (CD.siRNA) and co-formulated with a PEGylated lipid (CD.siRNA.DSPE-PEG) and a Fab (CD.siRNA.DSPE-PEG-Fab) targeting the CD123 receptor. Anti-leukaemia effects were investigated in KG1 cells using Wright-Giemsa staining (morphologic signs of differentiation) and using the Annexin V and propidium iodide assay (apoptotic cells). The PK of free siRNA, CD.siRNA, CD.siRNA.DSPE-PEG and CD.siRNA.DSPE-PEG-Fab were assessed after intravenous administration of a single dose containing 1.2 mg/kg FAM-siRNA in a total of 200 µl. The *in vivo* siRNA pharmacokinetic data in plasma was analysed by fitting to a one-compartment model.
Results and Discussion: The use of CD.DSPE-PEG-Fab NP containing BRD4-siRNA altered the morphology of KG1 cells from myeloblasts to cells with a monocyte-like appearance. In addition, the targeted BRD4-siRNA NPs achieved significantly ($P<0.05$) higher levels of apoptotic cells (Annexin V positive cells, ~ 30%) in comparison to those recorded by negative controls, i.e. targeted NP containing negative siRNA caused ~ 8% apoptotic cells. The PK studies indicate that PEGylated cyclodextrins enhanced the circulating times of siRNA compared to siRNA alone and siRNA in a non-PEGylated cyclodextrin NP.
Conclusion: The antibody-targeted cyclodextrin-based NP containing therapeutic siRNA is a novel therapeutic strategy with potential to treat AML and improve the circulating half-life of siRNA. Future work is underway to investigate the biodistribution and anti-cancer efficacy in an AML mouse model.

Acknowledgement of funding: We acknowledge the Irish Research Council for a Government of Ireland Postdoctoral Fellowship (GOIPD/2013/150).

Guo J, et al. Antibody-targeted cyclodextrin nanoparticles deliver siRNA and achieve therapeutic gene silencing in blood from acute myeloid leukaemia (AML) patients. 20th Congress of the European Hematology Association, 11-14 June, 2015, Vienna, Austria.

P: 30

Do Irish periodic paralysis patients have a common genetic origin?

Submitting Author: Collette Hand

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Discipline/Area: Department of Pathology, University College Cork

Abstract:
Periodic Paralyses (PPs) are rare autosomal dominantly inherited skeletal muscle channelopathies characterised by episodic weakness secondary to abnormal muscle excitability. PPs are classified into hyperkalaemic (HyperPP) or hypokalaemic (HypoPP) based on serum potassium (K^+) levels. HypoPP is caused by mutations in *CACNA1S* and *SCN4A;* HyperPP is generally caused by *SCN4A* gene mutations.

Following ethical approval, we have recruited a growing cohort of Irish PP patients for which comprehensive clinical and genetic data has been gathered. We believe that this group are phenotypically and genetically distinct. Firstly, contrary to publications, we have detected more HyperPP than HypoPP. Secondly, we have detected only one *SCN4A* gene mutation and finally, patients have unusual clinical features.

The aim of the study is to investigate this group of Irish HyperPP patients in which the same gene defect has been described and to determine whether there is a common genetic background. We generated a haplotype of the *SCN4A* gene region on chr17q in 10 HyperPP patients carrying a heterozygous *SCN4A* M1592V mutation and 6 mutation-negative controls. We identified a common genomic region among affected mutation-positive individuals that is absent in controls.

Findings suggest that the Irish HyperPP cohort recruited to date is unique in its clinical and genetic profile. This study provides evidence that *SCN4A* M1592V mutation carriers share a genomic region and supports a common genetic background. These results will influence the diagnosis and management of HyperPP patients.

This project was funded by the UCC School of Medicine **TRAP** and a Wellcome Trust Vacation Scholarship.

P: 31

Are we measuring modifiable risk factors in acute stroke patients

Submitting Author: Evelyn Hannon

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Discipline/Area: Departments of Geriatrics, Cork University Hospital, Cork

Abstract:
Stroke is a leading cause of death and disability [1]. Control of modifiable risk factors is the most effective approach to decreasing the burden of stroke[2-4]. The purpose of this study was to examine the frequency of measurement of modifiable risk factors in acute stroke patients admitted to Cork University Hospital (CUH). We conducted a retrospective review of the records of stroke patients admitted to CUH from 9th March 2014 to 9th March 2015. HbA1C, fasting glucose (FG), total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) measurements during admission were recorded. Among 445 strokes admitted to CUH, 388 (87%) were ischaemic. There was a mortality rate of 19% (n=83) at one month. Table 1 displays the frequency of measurement, and mean, of the modifiable risk factors examined in our study. Table 1: Over 80% of acute stroke patients had a measurement of cholesterol, and a test for diabetes mellitus performed. Current stroke guidelines recommend measurement of both LDL and HDL, which was performed in only 34% of our cohort[5].

Variable	Frequency: n (%)	Mean: mmol/l	Sd: mmol/l
HbA1c	241 (54%)	41.88	10.75
FG	252 (57%)	5.72	1.5
Either HbA1c or FG	383 (86%)		
TC	358 (80%)	4.52	1.23
LDL	150 (34%)	2.69	1.05
HDL	150 (34%)	1.79	.35
TG	334 (75%)	1.28	.71

LDL and HDL are not included in our standard lipid profile. This is an area of practice that needs to be re-examined.

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P: 32

Reducing Door to Needle Times for Ischaemic Stroke in Cork University Hospital (CUH)

Submitting Author: Evelyn Hannon

List of Authors: Hannon E, Byrne C, Healy L, Arrigan G, Gallagher P, Cronin S.

Discipline/Area: Departments of Geriatrics and Neurology, Cork University Hospital

Abstract:
Background: "Time is Brain" is true in stroke thrombolysis. There is a 4.5hr time window from stroke onset to thrombolysis administration and improved outcomes with earlier delivery. In Helsinki, interventions to reduce the Door to Needle Time (DNT) have resulted in 94% of patients being treated within 60 minutes of arrival to hospital and a median DNT of 20 minutes in 2011.[1] Our aim was to analyse our thrombolysis pathway and DNT to identify improvements that could be made locally.

Method: A retrospective analysis of patients' charts was performed. All 45 patients in Cork University Hospital thrombolysed for Acute Ischaemic Stroke, from July 2014 to June 2015, were included. Data was analysed as median DNT in minutes with an interquartile range.

Results: The median DNT was 82 minutes (66-106). 11% (4/45) were treated within 60 minutes. In hours median DNT was 68 minutes (60-82) and out-of-hours median DNT was 88 minutes (73-116). When seen by a specialty doctor on arrival the DNT was 62 minutes (50-68) as compared to 85 minutes (73-116) when seen initially by a non-specialty doctor. Consultant review in person, blood pressure control, advanced imaging and time from stroke onset did not significantly affect DNT.

Discussion: The target of thrombolysis within 60 minutes was not achieved in the vast majority of patients. We have identified potential areas of improvement and aim to instigate changes to our stroke thrombolysis pathway to achieve the target.

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P: 33

Appropriate Use of Elective Coronary Angiography in Patients attending Cork University Hospital with suspected Coronary Artery Disease

Submitting Author: Michael Hanrahan

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(2) Department of Cardiology, Cork University Hospital, Cork

Abstract:
Background: Coronary angiography is an important step in the diagnosis and management of Coronary Artery Disease (CAD). The potential inappropriate use of this procedure is an increasing concern. Appropriate Use Criteria have been developed by the American College of Cardiology (1) to aid patient selection for coronary angiography. The purpose of this study was to apply these criteria retrospectively to patients who underwent elective outpatient coronary angiography for suspected stable CAD in Cork University Hospital (CUH) and investigate the levels of appropriate use.

Methods: Inclusion criteria: CUH outpatients who underwent elective coronary angiography between 1/1/2014 and 31/12/2014. Exclusion criteria: emergency/ urgent indications, previous myocardial infarction, coronary artery bypass graft, percutaneous coronary intervention, known CAD from previous coronary angiography, and coronary angiography prior to other surgery. Appropriate use was scored on the basis of prior non-invasive testing or pre-test probability of CAD/ Global CAD Risk Score (GRS). Multivariate analysis adjusted for gender, age, BMI, smoking history, pay authority, symptoms, atrial fibrillation and blood pressure.

Results: 259 patients were included in this study. 41.7% were rated as appropriate, 20.8% as inappropriate and 37.5% as uncertain. The odds of finding obstructive CAD was 2.29 (95% CI 1.04 – 5.07) times as likely in those rated as appropriate as those rated as inappropriate. In an adjusted multivariate logistic regression model private patients were significantly more likely than public patients to undergo coronary angiography for an appropriate indication vs. inappropriate/uncertain indication (adjusted OR 2.21 [95% CI 1.24 – 3.97]).

Conclusions: The diagnostic yield of coronary angiography was relatively low in this study and this could be improved with better patient selection and risk stratification using the Appropriate Use Criteria, exercise stress testing and GRS.

Ethical Approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals.

Funding: Association of Physicians of Great Britain and Ireland Intercalated Degree Scholarship.

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P: 34

Hepatitis C Regulates the Expression of ATG5

Submitting Author: Ciara Harty

List of Authors: Harty C.H (1), Crosbie O (2), Kenny-Walsh E (2), Fanning L.J (1)

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(2) Hepatology, Cork University Hospital.

Discipline/Area: Molecular virology diagnostic and research laboratory, Department of Medicine, University College Cork, Cork

Abstract:
Autophagy is a complex pathway involved in recycling cellular components. It is reported that ATG5 is essential for HCV replication (1). HCV may utilise ATG5 as a proviral factor at the onset of viral infection. We sought to clarify the role of ATG5 in the life cycle of HCV using a human serum-derived HCV. We have developed an *in vitro* infection model for serum derived HCV (sdHCV). The inability of HCV to complete a full cycle of replication *in vitro* is well established. For this reason, there has been limited use of sdHCV in cell culture. However, we have shown the presence of HCV core protein in Huh7 cells using western blotting and immunofluorescence using sdHCV. qPCR was used to determine the levels of intracellular HCV RNA.

Intracellular HCV RNA increased over the initial twenty hour infection period. sdHCV has the ability to gain entry into the cells, the incoming RNA is translated into protein but is not replicated. The model mirrors *de novo* infection of naïve Huh7 hepatocytes. We have shown that sdHCV infection causes no change in the mRNA but protein levels of ATG5 are increased. mRNA levels of ATG5 are unchanged in HCV replicon cells (representative of a chronic infection state); however, ATG5 protein expression is increased as compared to controls. This indicates the initial stages of HCV infection and HCV RNA replication upregulate ATG5 protein expression by translational control. Investigation into the 5'UTR translational control of ATG5 is on-going.
Ethical approval was acquired from the Clinical Research Ethics Committee of the Cork Teaching Hospital.

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P: 35

Assessment of autophagy inducers and differentially expressed genes as modulators of chemo-sensitivity in oesophageal cancer

Submitting Author: Michael Healy

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Discipline/Area: Cork Cancer Research Centre, Biosciences Institute, Cork, Ireland

Abstract:
Autophagy is a highly conserved cellular process, whereby components of the cytoplasm, such as protein aggregates, organelles and other macromolecules are digested. Our laboratory has previously shown that while chemo-sensitive cell lines (OE21 & OE33) display apoptotic cell death in response to treatment with 5-fluorouracil (5-FU), chemo-resistant oesophageal cancer cell lines (OE19 & KYSE450) only induce autophagy [1].

Potential inducers of autophagy have been screened and tested to see if disruption of this process can chemo-sensitise resistant cells to 5-FU. Affymetrix GeneChip® array data was also examined to assess differential gene expression between the chemosensitive and resistant cell lines.

LC3II levels and clonogenic survival assays were used to determine the effect a number of compounds (amiodarone, trehalose, carbamazepine and valproic acid (VPA)) on autophagy induction and chemo sensitisation to 5-FU. VPA (2.5mM & 5mM) as a single agent, negatively impacted clonogenic survival of KYSE450 cells. When tested in combination with 5-FU, valproic acid displayed a synergistic effect in decreasing clonogenic survival. The contribution of autophagy to this enhancement of cytotoxicity with these agents is currently under evaluation.

Using various inclusion criteria and data mining of gene databases, we selected and confirmed differential expression of several genes (SYT1, TNFAIP3, PRKCA, Trim24 & NT5E). siRNA knockdown was then used to determine their potential roles in cell survival.

Valproic acid in combination with 5-FU may represent a novel treatment strategy for chemo-resistant oesophageal cancer cells. Knockdown studies have shown that SYT1 mRNA levels can significantly affect cell susceptibility to 5-FU.

P: 36

Smad-interacting protein 1 is a novel regulator of nigrostriatal pathway development, and a therapeutic target for Parkinson's disease

Submitting Author: Shane Hegarty

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Discipline/Area: Department of Anatomy and Neuroscience, University College Cork

Abstract:
Ventral midbrain (VM) dopaminergic (DA) neurons project to striatum via nigrostriatal pathway to control voluntary movement. Progressive neurodegeneration of nigrostriatal pathway causes the incurable Parkinson's disease (PD). In PD, there is an extended pre-symptomatic period due to compensatory neurite growth of remaining nigrostriatal DA neurons, which maintain striatal innervation until >70% of neurons degenerate. Understanding the, as yet uncharacterised, molecular mechanisms regulating nigrostriatal pathway development may identify novel therapeutic targets to protect, maintain and/or restore nigrostriatal DA innervation in PD.

Smad-interacting protein-1 (Sip1) transcription factor is a negative regulator of bone morphogenetic protein (BMP)-Smad signalling, and is a multifunctional regulator of nervous system development[(1)]. BMPs act as neurotrophic factors for VM DA neurons, signalling via Smads to promote DA neurite growth[(2)]. siRNA-mediated Sip1 knockdown promotes neurite growth in SH-SH5Y neuronal cell line and in primary cultures of rat VM DA neurons. Neurite growth induced following Sip1 knockdown is prevented by Smad knockdown, or inhibition of BMP receptor activation, suggesting that de-repressed BMP-Smad signalling promotes DA neuronal growth in the absence of Sip1. Indeed, *Sip1* expression is upregulated by BMPs in VM DA neurons and SH-SH5Y cells, and may participate in negative feedback regulation of BMP-Smad-promoted DA neuronal outgrowth. Characterisation of *in vivo* VM expression profile of Sip1 during nigrostriatal pathway development showed that Sip1 expression decreases during VM DA neuronal outgrowth and target innervation, when expression of BMP ligands and receptors increases. These data suggest that Sip1 regulates nigrostriatal pathway development through negative regulation of BMP-Smad-promoted VM DA neuronal outgrowth.

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P: 37

Regulation of Myelination in the Prefrontal Cortex by the Microbiota

Submitting Author: Alan Hoban

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Discipline/Area: Department of Anatomy and Neuroscience, University College Cork

Abstract:
Background: Myelination is a critical but vulnerable dynamic feature of normal brain development with implications for mental health and disease ranging from neurodegenerative to chronic stress disorders and multiple sclerosis. In particular, normal cognition and social functioning appear to be contingent on intact myelination in the prefrontal cortex (PFC), a brain region implicated in multiple psychiatric disorders. Interestingly, social isolation stress results in a decreased myelination in the (PFC). Growing evidence points to a role for the gut microbiome in regulating brain function and behaviour. Studies in germ-free (GF) animals, have highlighted the impact the microbiota can have on neurodevelopment with GF animals demonstrating decreased sociability. Given these overlaps, we aimed to investigate whether GF mice displayed altered myelination in adulthood in this brain region.

Methods: We assessed both at the ultrastructural and transcriptional level changes in myelin sheath thickness and functional myelin sheath components using transmission electron microscopy and qRT-PCR.

Results: Ultrastructural analysis revealed hypermyelination within the PFC of GF mice as indicated by decreased g-ratio compared to conventional mice. These mice also displayed increased expression of six myelin genes only within the PFC. However, colonisation post-weaning normalised the expression of these myelin component genes. Coinciding with this, GF mice displayed altered expression of oligodendrocyte regulating genes within the PFC.

Conclusion: This is, to our knowledge, the first demonstration that the gut microbiota can regulate myelination. This effect is brain-region specific. Moreover, our results suggest that the microbiota can be successfully targeted later in life to modulate myelination patterns, at least at the transcriptional level. This raises the possibility that targeting the gut microbiota during critical time windows could be a viable approach for treating disorders associated with abhorrent myelination patterns.

P: 38

HSPA 5 as Biomarker for Early Diagnosis of Diabetic Nephropathy

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Discipline/Area: School of Medicine, University College Cork

Abstract:
Background: Diabetic nephropathy is responsible for 20-44% of all end stage renal diseases among 43 countries reported to US Renal Data System in 2006. Current method use urinary albumin level and eGFR for diagnosis of diabetic nephropathy (2) and lack the ability to detect early injury and do not predict disease progression accurately. HSPA5 is an endoplasmic reticulum protein and a member of the HSP70 family. HSPA5 expression is regulated by hyperglycaemia and is increased in tubule-rich renal biopsies from patients with diabetic nephropathy compared with control subjects (3).

Aim: This research aims to investigate the use of HSPA 5 as biomarker for early diagnosis of diabetic nephropathy.

Methods: Urine samples were collected from patients with diabetes and from patients with chronic kidney disease following patient consent and with ethical approval from Cork University Hospital. HSPA5 protein was measured in urine from 27 diabetic patients, 4 of whom had nephropathy, and 33 non-diabetic patients with chronic kidney disease by dot blot analysis. HSPA5 protein in twenty of these samples (ten from each cohort) was also measured by western blot analysis.

Results: HSPA5 protein was detected in urine from both diabetic and CKD patients by dot blot analysis however signal intensity varied suggesting that HSPA5 may correlate with kidney function. Western blot analysis indicated that HSPA5 protein is abundant in the urine of patients with CKD and diabetic nephropathy, consistent with the findings from the dot analysis. Two patients with diabetes but without diagnosed kidney disease also had detectable HSPA5 protein in their urine, suggesting that HSPA5 may be a biomarker for early disease.

Conclusion: These experiments indicate that HSPA5 is readily detected in urine of patients with chronic kidney disease and may correlate with disease severity. Further studies are required to determine whether HSPA5 may be used as a biomarker for early diagnosis of diabetic nephropathy.

Funding: Wellcome Trust Biomedical Vacation Scholarship

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P: 39

Lentiviral overexpression of interleukin-1β in the hippocampus induces neurogenesis-associated cognitive deficits in adult male rats

Submitting Author: Cara M.Hueston

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Discipline/Area: Department on Anatomy and Neuroscience, University College Cork

Abstract:
Previous studies have demonstrated that elevated levels of the pro-inflammatory cytokine interleukin-1β (IL-1β) in the hippocampus has detrimental effects on memory and cognitive function, as well as on the proliferation and survival of newly born neurons. The current study aimed to assess whether long-term lentiviral-mediated overexpression of IL-1β would alter performance in a series of hippocampal-dependent tasks including pattern separation, which has previously been demonstrated to be dependent on hippocampal neurogenesis. A lentivirus overexpressing IL-1β ($3.7x10^3$ TU) or mCherry as a control was bilaterally injected into the dorsal hippocampus of adult male Sprague-Dawley rats. Three weeks after injection a battery of behavioural tests were carried out. Hippocampal tissue was collected 4 days following behavioural testing for analysis by real-time RT-PCR for changes in gene expression levels of IL-1β and neurogenesis-related markers. Increased mRNA expression of IL-1β was confirmed in the hippocampus following lentiviral IL-1β overexpression. In the pattern separation task, rats overexpressing IL-1β in the dorsal hippocampus were not able to pattern separate in the small separation condition, but were able to do so with a large separation, suggesting hippocampal neurogenesis-associated dysfunction. The current results indicate that long-term hippocampal exposure to the pro-inflammatory cytokine IL-1β has detrimental effects on the neurogenesis-associated pattern separation cognitive task. Thus, the ability to pattern separate may be more susceptible to the detrimental effects of chronic inflammation than other hippocampal-dependant functions such as working memory and location recognition memory.

All animal procedures were performed under licenses issued by the Health Products Regulatory Authority (HPRA, Ireland), in accordance with the European Communities Council Directive (86/609/EEC).

Funding: SFI grant 12/IA/1537 to YMN and JFC.

P: 40

Detecting the microbiome of the asthmatic lung

Submitting Author: Eoin Hunt

List of Authors: Hunt EB (1,2,4), Lapthorne S (1), Ward C (3), Eustace J (4), Plant BJ (2,4), Murphy DM (2,4)* , MacSharry J (1)*

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(2) The Department of Respiratory Medicine, Cork University Hospital, Cork, Ireland.
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**= Joint Supervisors*

Discipline/Area: Schools of Medicine and Microbiology, APC Microbiome Institute, University College Cork, Ireland

Abstract:
Until recently, the lower airways were thought to be sterile unless infected; however, a shift towards molecular methods for the quantification and sequencing of bacterial DNA has revealed that the airways harbour a microbiota. These new techniques have changed the way that respiratory research is approached, with a need now to consider the effects of host–microorganism interactions in both healthy and diseased lungs.

Our aim was to detect the Lower airway microbiota using both molecular and microscopic techniques in an Irish cohort of well-defined asthmatics
76 asthmatic patients underwent bronchoscopic investigation and bronchoalveolar lavage (BAL), ACQ7, FENO, IgE/RAST blood tests and spirometry in order to clinically characterize their disease severity. Molecular techniques including quantitative polymerase chain reaction (qPCR) were employed to detect microbial species in the BAL.

Our results to date suggest a shift in the presence of Firmicutes (71%) (Streptococci/Staphylococci), and Proteobacter especially those of clinical importance (Pseudomonas (54%), Bordetella (54%) and Escherichia (69%)), compared to reported research for the normal lung. The presence of Prevotella (69%), normally found in the oropharynx and GI tract is of clinical interest with regards to gastric reflux, which is well described in this clinical population. We have also observed an increased presence of Aspergillus (71%), which is underreported in the asthma population to date.

Our results demonstrate a shift in lung microbial species in Asthma. It is unclear how this change in microbes contribute to asthma phenotype.

Funding for this project has been provided by the Wilton Research fund and a HRB summer studentship.
Ethical Permission has been granted for these studies.

P: 41

Microbiota Regulation of Bladder Toll-like Receptor Expression in Male and Female Mice

Submitting Author: Niall Hyland

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Discipline/Area: APC Microbiome Institute and Department of Pharmacology & Therapeutics, UCC

Abstract:
Toll-like receptors (TLRs) are pattern recognition receptors which recognise molecular patterns displayed by microorganisms. Evidence suggests that altered TLR-mediated responses are associated with bladder pain syndrome (BPS; 1). Moreover, evidence also suggests that the bladder microbiome may be altered in BPS (2). However, the influence of the microbiota on bladder TLR expression has not been examined. We assessed TLR2, TLR4 and TLR11 receptor gene expression, the latter of which protects against uropathogenic infection in rodents, in mouse bladder. Bladder tissue was obtained from male and female conventional (Conv) and germ-free (GF) mice, and GF mice subjected to microbiota colonisation. Real-Time RT-PCR was carried out using probes to mouse *Tlr2*, *Tlr4* and *Tlr11* genes (Integrated Life Technologies™). Fold-change in expression levels relative to conventional tissues were analyzed and data expressed as mean ± SEM. Statistical differences were determined by two-way ANOVA and Bonferroni post-hoc test. *Tlr2* receptor expression was significantly influenced by microbiota colonisation in female mice ($P<0.05$). An approximate 50% reduction in *Tlr11* expression was also observed in female colonised mice. No changes in the expression of *Tlr2*, *Tlr4* or *Tlr11* were observed in any of the male experimental groups or in germ-free female mice. No significant interaction between microbiota status and sex with respect to *Tlr* expression was identified. These data suggest that TLR2, and to a lesser degree TLR11, receptor expression display sensitivity to microbiota colonisation in a sex-dependent manner.

We acknowledge support from the Translational Research Access Programme (**TRAP**), UCC.

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P: 42

Clinical outcome in patients with functional neurological symptoms: A 4-year follow-up study

Submitting Author: Mobin Jamel

List of Authors: Jamal M, Gaughan M, O'Sullivan S

Discipline/Area: Department of Neurology, UCC, Cork

Abstract:
Patients with functional symptoms make up a large proportion of an average neurologist's workload (1, 2). These patients are, on the criteria of distress, disability and persistence of symptoms, as deserving as patients with pathologically defined disease. Management of functional neurological symptoms focuses on early diagnosis, psychiatry review and physiotherapy for motor symptoms. Previous research in this area suggests poor long-term outcomes for those with functional neurological symptoms and, in terms of the Irish population, no data currently exists (3). This study followed up on a cohort of patients diagnosed with functional neurological illness and referred to psychiatry in 2011, aiming to identify patient factors and treatment strategies that predict better outcomes. Using a GP questionnaire to collate data, we focused on three outcome measures: (1) resolution of symptoms; (2) frequency of GP attendance; and (3) development of new symptoms. Of the 31 patients identified in 2011, only 7 GPs reported resolution in the symptom(s) of their patient in 2015. There was no strong association between age, gender or premorbid employment status and resolution of symptoms. Interestingly, patients who frequently attended their GP did not tend to develop new neurological symptoms, however frequent GP attendance may suggest ongoing somatization. All 5 of the patients who developed new symptoms seemed to have a previous documented psychiatric diagnosis. The results suggest that current best practice treatment strategies may not be entirely effective in resolving functional neurological symptoms (7/31).

This project has received ethical committee approval.

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P: 43

Mouse Models of the Microbiome in Colorectal Cancer.

Submitting Author: Jonathan Keane

List of Authors: Jonathan Keane, Aileen Houston, Cormac Gahan, Niall Hyland, Susan Joyce, Pat Casey, Silvia Melgar, Sarah-Louise Long, Fergus Shanahan

Discipline/Area:

Abstract:
Two different mouse models can be applied to investigate familial and sporadic colorectal cancer (CRC). For the most part these models are characterized with respect to endpoint or disease state. My project aims to investigate disease risk and delimit causative and consequential factors of CRC. As a model for sporadic cancer, C57BL/6J mice are exposed to genotoxic azoxymethane (AOM) by in**TRAP**eritoneal injection causing tumours in the distal colon [1]. As a model for familial cancer, APCMIN mice carry a nonsense mutation in the tumour-suppressor *Apc* gene, also seen in humans suffering from familial adenomatous polyposis (FAP). These mice develop hundreds of polyps in their small intestine [2].
These models are being applied to examine the role played by both the microbiota and metabolites in CRC risk, initiation and progression. Alteration in the composition of the microbiota and metabolites are documented in CRC [3]. Currently, faecal samples are being collected from both mouse models over the course of tumour development to track changes in the faecal-associated microbiota and metabolites. This is combined with timed culls to monitor disease state. Subsequently, we will perform intervention studies by pre-treating mice with antibiotics and exposing them to bacteria of interest via drinking water. These may be bacteria associated with tumour development or part of certain metabolic pathways and may be wild-type or engineered to carry genes of interest.
Funding provided by the APC Innovation Platform. Animal experiments were conducted in accordance with the regulations and guidelines of the Irish Department of Health and protocols were approved by the University College Cork Animal Experimentation Ethics Committee.

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P: 44

Barriers and facilitators associated with attending community-based interventions among families of overweight and obese children

Submitting Author: Emily Kelleher

List of Authors: Kelleher E, McHugh S, Shiely F, Davoren M, Perry IJ, Harrington JM.

Discipline/Area: Department of Epidemiology and Public Health, University College Cork

Abstract:
Evidence suggests multi-component family-based lifestyle programmes are efficacious in treating paediatric obesity (1). However, success relies heavily on family attendance and retention (2). While attendance offers the support to make long-lasting, positive, lifestyle changes, in addition to the opportunity to identify underlying medical, behavioural or mental health issues, the majority of families referred to treatment decline (3). Moreover, for those who do attend, benefits are often compromised by high programme attrition (1). While non-attendance directly impacts on the children and their families, it also negatively impacts the health service due to missed appointments and loss of productivity (4). This systematic review aimed to investigate the factors influencing attendance at community-based lifestyle programmes among families of overweight or obese children. Quantitative, qualitative and mixed-methods studies were included. A narrative synthesis approach was used to allow for inclusion of a range of research designs. Thirteen studies were included. Predictors of attendance varied greatly. Children enrolled to improve their weight and appearance and to have fun. However, the stigma associated with attending these programmes discouraged others. For parents, the main factors influencing enrolment included concern for their child's health, the desire to reduce bullying and to increase their child's self-confidence. Logistical factors such as time, transport, conflicting schedules and changing family circumstances influenced families' decisions to drop out of treatment. Group support and the structured environment encouraged continued attendance. In conclusion, strategies to boost recruitment and avoid and minimise attrition are urgently required to optimise the effectiveness of childhood obesity treatment in the community setting.

This research was funded by the Health Research Board SPHeRE/2013/1.

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P: 45

Transferring the Blues: Depression-Associated Gut Microbiota Induces Neurobehavioural Changes in the Rat

Submitting Author: John Kelly

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(5) Department of Anatomy and Neuroscience, University College Cork

Discipline/Area: APC Microbiome Institute and Department of Psychiatry and Neurobehavioural Science, UCC

Abstract:
The gut microbiota is a complex metabolic ecosystem, which interacts with the host via neuroimmune, neuroendocrine and neural pathways [1][2] . These pathways are integral components of the brain-gut-microbiota axis and pre-clinical evidence suggests that the microbiota can recruit this bidirectional communication system to modulate brain development, function and behaviour [3]. Although it is well acknowledged that the pathophysiology of depression involves neuroimmune-endocrine dysregulation, the extent to which changes in the gut microbiota composition and function mediate dysregulation of these pathways in depression is currently unknown.

We demonstrate that depression is associated with altered gut microbiota richness and phylogenetic diversity. Moreover, we show that fecal microbiota transplantation from depressed subjects to microbiota-deficient rats can induce the development of behavioural and physiological features of depression in the recipient animals. This includes anhedonia and anxiety like behaviours, as well as alterations in tryptophan metabolism.

This suggests that the gut microbiota may play a causal role in the development of features of depression and may provide a tractable target in the treatment and prevention of depression.

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P: 46

TLX, a regulator of neurogenesis, is required for microglial in the adult mouse hippocampus

Submitting Author: Danka A. Kozareva

List of Authors: Danka A. Kozareva, Cara M. Hueston, Ciarán S. Ó'Léime, John F. Cryan, Yvonne M. Nolan

Discipline/Area: Department of Anatomy and Neuroscience, University College Cork, Ireland

Abstract:
Tailless homolog TLX (Nr2e1) is an orphan nuclear receptor expressed primarily in the neurogenic niches of the adult mouse brain including the dentate gyrus of the hippocampus, and is involved in the regulation of neurogenesis (birth of new neurons). Hippocampal inflammation has been implicated in the pathology of many neurodegenerative and psychiatric disorders including Alzheimer's disease and stress-induced depression. Alterations in adult hippocampal neurogenesis have also been implicated in these disorders. Our aim is to understand the relationship between inflammation, TLX expression and adult hippocampal neurogenesis. In order to explore the interaction between TLX and inflammation, we assessed microglial morphology and hippocampal architecture in mice which had a spontaneous deletion of Nr2e1 ($Nr2e1^{-/-}$). Immunohistochemistry was performed to compare the number of microglia ($Iba1^{+}$ cells) and number of newborn neurons (DCX^{+} cells) in the hippocampus of these mice compared to their wild type littermates. The activation status of microglial cells in the hippocampus of these mice was also established. We observed a marked discrepancy in the integrity of the dentate gyri of the hippocampi in $Nr2e1^{-/-}$ mice compared to wild type mice. Furthermore, a lack of TLX expression led to reduced numbers of newly born neurons in the adult mouse dentate gyrus as well as altered microglial morphology. Our current findings suggest that TLX is necessary for intact neurogenic cells as well as having a role in the maintenance of endogenous microglial integrity.This material is based upon work supported by the Science Foundation Ireland under Grant No. SFI/IA/1537. All experiments were conducted in accordance with the European Directive 2010/63/EU, and under an authorization issued by the Health Products Regulatory Authority Ireland and approved by the Animal Ethics Committee of University College Cork.

P: 47

Identification of mucosal and systemic markers for categorisation of Asthmatic patient severity

Submitting Author: Susan Lapthorne
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(3) The HRB Clinical Research Facility, University College Cork, Cork
#= equal contribution
**= Joint Supervisors*

Discipline/Area: Schools of Medicine and Microbiology, APC Microbiome Institute, University College Cork

Abstract:
The worldwide incidence of asthma is increasing and in Ireland the prevalence is now estimated at 470,000. In asthma there is dysregulation of the airway immune system, leading to hyperresponsiveness and remodelling of the airways and the clinical manifestation of the disease.

To characterise the immune cell phenotype and cytokines in bronchoalveolar lavage (BAL) fluid of patients with asthma and to compare this to systemic markers of inflammation and disease severity.

Patients with asthma were assessed for severity by ACQ7, FEV1 and GINA and subsequently underwent bronchoscopy, BAL and peripheral venous blood collection. A differential cell count was performed and pro-inflammatory cytokines in the BAL fluid were measured using MSD-ELISA. Full blood cell count and CRP analysis was performed.

The BAL cytokine IL-1β positively correlated with increased BAL neutrophils (n=47). BAL IL-6 correlated with increased total white cell count, neutrophils and increased GINA score. IL-8 correlated with elevated BAL neutrophils and systemic CRP. BAL eosinophils correlated with increased BAL IL-5. BAL IL-17 correlated with disease severity, decreased FEV1 and increased ACQ7 score.

BAL IL-6 levels reflect patient systemic inflammation in particular associated with blood neutrophils. BAL IL-17 is associated with a more severe asthmatic phenotype and compromised lung function. These observations may help in defining the severity of patient asthmatic status.

Funding for this project has been provided by the Wilton Research fund and a HRB summer studentship.
Ethical Permission has been granted for these studies.

P: 48

Corticosterone differentially affects neural progenitor cells derived from specific areas of the longitudinal axis of the hippocampus

Submitting Author: Bruno Rocha Levone

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Discipline/Area:

Abstract:
Adult hippocampal neurogenesis (AHN) plays important roles in learning, memory, anxiety and the response to stress and antidepressants. How AHN plays a role in processes as diverse as spatial learning and the stress response is currently unclear. However, accumulating evidence suggests that the hippocampus is functionally segregated along its longitudinal axis such that the dorsal hippocampus (dHi) plays a preferential role in spatial learning and memory, while the ventral hippocampus (vHi) plays a preferential role in the stress response. Recent studies in our lab suggest that stress and antidepressants preferentially affect neurogenesis in the vHi rather than the dHi. The aim of this study was to determine whether neural precursor cells (NPC) derived from specific areas along the longitudinal axis of the hippocampus differentially respond to corticosterone, a hormone that is released during stress. To this end, NPCs were prepared from the rat dHi, vHi and intermediate hippocampus (iHi) and the effects of corticosterone on proliferation and neuronal differentiation was examined. Corticosterone reduced cell proliferation irrespective of the region the NPCs were derived from. MTT assays showed that corticosterone-induced reductions in proliferation were not due to reduced cell viability. Corticosterone also reduced neuronal differentiation and maturation. However, newly-generated neurons from vHi NPCs were less sensitive to corticosterone-induced impairments in maturation and matured faster than those from the dHi or vHi. These findings suggest that stress-induced reductions of neurogenesis in the vHi *in vivo* are unlikely to be due to increased sensitivity of vHi NPCs to the stress hormone corticosterone.

BRL is supported by the National Council for Scientific and Technological Development (CNPq) of Brazilian government (Grant number 249007/2013-4).

P: 49

Development of a cranial nerve animation to enhance dental student learning

Submitting Author: Mutahira Lone

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Discipline/Area:

Abstract:
The structure and function of the cranial nerves is a core topic for dental students but due to the complexity of the topic, it is difficult to develop a good understanding by exclusively using textbooks and models. It is generally accepted that the acquisition of anatomical knowledge can be facilitated by visualization of structures [1]. The aim of this study is to assess a new animation as a learning aid for first-year dental students. A cartoon-type animation detailing the names, roles and anatomy of the cranial nerves with particular emphasis on a life scenario was developed based on Mayer's theory of multimedia learning[2]. Questionnaires were designed to assess the participants' knowledge of the cranial nerves before and after visualization of the animation. Following consent, the participants completed the "pre-animation" questionnaire and observed the animation in a lecture theatre (n=49). The participants had continued access to the animation for 2 weeks after which they completed the "post-animation" questionnaire.

Results from the pre-animation questionnaire showed that although more than half the respondents (57.1%; n=28) had heard of the cranial nerves, the majority (87%, n=43) stated they had little knowledge of cranial nerves and indeed could not associate them with their functions. The majority of respondents (87.7%; n=43) felt that animations are helpful tools in understanding anatomy and can be beneficial in teaching difficult topics (94%; n=46). Pending the post-animation questionnaire, this study suggests that this new animation of the cranial nerves will facilitate the visual and 3D understanding the cranial nerves and their functions.

This study was funded by a teaching grant from the Dental School and Hospital, UCC. Social Research Ethics Committee (SREC) approval was obtained for the study.

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P: 50

Rational selection of Lactobacillus strains based on bile salt hydrolase activity.

Submitting Author: Sarah L. Long

List of Authors: Sarah L. Long (1,2), Fergus Shanahan (1), Cormac G. M. Gahan (1,2,4), Susan A. Joyce (1,3)

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Discipline/Area: APC Microbiome Institute and School of Microbiology, University College Cork

Abstract:
Lactobacillus species form an integral part of the human gut microbiome. They are frequently applied as probiotics with the prerequisite that they can metabolize bile acid (BA). Bile salt hydrolase (BSH) enzymes are the gateway reaction for BA metabolism by gut microbes [1]. BSH removes a glycine or taurine moiety conjugated to a bile acid yielding free BAs, these can then be subsequently further microbially modified. These modifications can result in alterations in host physiology [3]. Within the *L.salivarius* species alone allelic variation of the BSH proteins have been divided into four major groups, all of which have distinct differences [2], one of these has been shown to be a significant factor in the reduction of host weight gain[3]. This study applied rational selection and screening to isolate and identify new strains of *Lactobacillus* with BSH enzymes with specific activities. Six isolates, of either pig or human origin, were characterized genetically and phenotypically, for their ability to alter BAs and for their physiological effect on the murine host. Their potential in conferring health benefits is discussed.

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P: 51

The microbiota shapes amygdala volume and dendritic morphology

Submitting Author: Pauline Luczynski

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Discipline/Area: APC Microbiome Institute, University College Cork

Abstract:
Germ-free mice (GF) have provided critical insights into the role of the microbiota in the regulation of the central nervous system (CNS). Amygdala-mediated responses including stress hormone signalling, anxiety-like behaviour and sociability are altered in GF mice. While the mechanisms underlying this behavioural and physiological profile have yet to be elucidated, it is possible that the microbiota recruits structural aspects of the amygdala to mediate its effects on the CNS. Therefore, the aim of the present study was to determine if the volume and dendritic morphology of the amygdala differ in GF compared to conventionally colonized mice. Stereological measures of amygdalar nuclei revealed that the basolateral (BLA), lateral and central nuclei were all enlarged in GF mice. We also investigated microbiota-induced changes at the level of single excitatory (pyramidal-like) and inhibitory (stellate) neurons in the BLA by measuring the dendritic length, branching and spine density. In GF mice, stellate neurons were significantly longer and more branched. Pyramidal-like neurons of GF mice were longer and had more spines but did not differ in branching compared to controls. These findings suggest that the amygdala is a brain region whose structural integrity is contingent on the presence of a gut microbiota and that neural remodelling may underlie the altered stress responsivity and sociability of GF mice.

All experiments were approved by the Animal Experimentation Ethics Committee of UCC.
The authors are funded by Science Foundation Ireland (SFI/12/RC/2273), by the Health Research Board (HRA_POR/2012/32 and HRA_POR/2014/647) and through EU GRANT 613979 (MYNEWGUT FP7-KBBE-2013-7).

P: 52

A Multi-Disciplinary Quality Improvement Project Aimed at Reducing Avoidable Readmissions Through Improved Discharge Processes

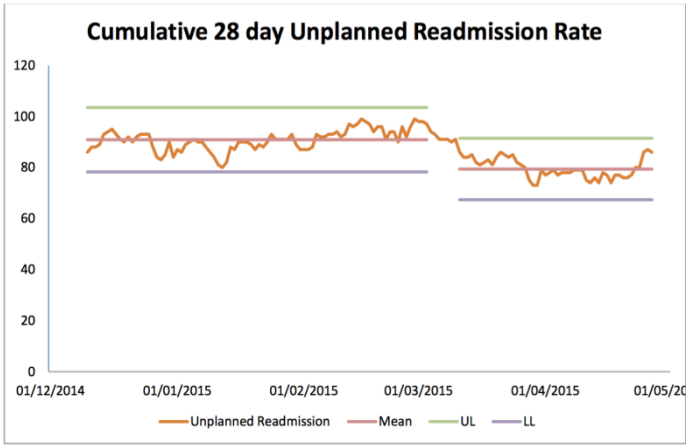
Submitting Author: Keith McGrath

List of Authors: McGrath K, Donovan K, Holland R, McKiernan M, O' Connor K

Discipline/Area: Mercy University Hospital

Abstract:
Readmissions are costly for healthcare and undesirable for patients. Hospitals with low readmission rates ensure smooth transitions as their patients are discharged. Our aim was to reduce avoidable readmissions by improving the discharge process in our hospital. We collected quantitative & qualitative data using a mixed methods research approach. Information from patients, carers, and staff was gathered through structured and unstructured interviews. Factors influencing our aim were represented on a driver diagram. Causes of deficiencies in the current discharge process were displayed on a fishbone diagram. Quality Improvement interventions based on these were tested and introduced by rapid Plan-Do-Study-Act cycles. We developed a measurement dashboard comprising relevant run charts to assess improvement. Our results indicate that 1/3 of 28-day readmissions were potentially avoidable. Some reasons for avoidable readmissions were not within a hospital's control. Nevertheless, the majority of reasons related to inadequate discharge planning. During our project a "multidisciplinary discharge planning checklist", a pathway for frail older patient assessment, a "complex discharge round", and educational sessions on discharge planning were introduced. Individualised discharge plans and early telephone follow-up for complex discharges commenced. Avoidable readmissions reduced by 25%.

The overall rate of 28-day readmissions fell from 9.8% during baseline period to 8.1% by the end of the project. Reducing avoidable readmissions has great potential to improve quality and lower spending throughout the healthcare service. Readmissions can be reduced by improving discharge planning processes. A person-focused approach is crucial in understanding the unique issues of each high-risk individual admitted to the hospital.



P: 53

Malignant Pleural Effusions: Current differential diagnosis, management and outcome

Submitting Author: Paul McGrath

List of Authors: McGrath PA, McCarthy J, Chawke L, Arooj P, O'Connor TM, Curran D, Henry MT, Kennedy MP

Discipline/Area:

Abstract:
Background:
Malignant Pleural Effusion (MPE) is a common condition among cancer patients mainly affecting breast and lung cancer patients but they can occur in any malignancy. As part of an initiative to streamline the management of MPE, we performed a retrospective review of management and outcomes of MPE in our institutions.

Methods:
All positive thoracentesis samples analysed in the CUH Cytology lab over a two year period were included (2012-2013). With institutional approval, a retrospective chart review was thereafter performed.

Results:
MPE occurred in 82 patients (40 Male, 42 Female, n=20 with repeat samples) with an average age of 67 Years. Lung Cancer is the leading cause of MPE's accounting for 46% of cases. Video assisted thoracoscopic surgical (VATS) pleurodesis accounts for 46% of treatments for MPE in our institutions.

Conclusion:
At present, the majority of patients with MPE in our institutions survive more than three months and the most common treatment is VATS talc pleurodesis.

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P: 54

Improving diabetes care in Ireland: a realist evaluation of the National Clinical Programme for Diabetes

Submitting Author: Sheena McHugh

List of Authors: McHugh, S, Tracey, T, Riordan, F, O'Neill, K, Kearney P.M.

Discipline/Area: Department of Epidemiology & Public Health, UCC, Cork

Abstract:
Our aim is to conduct a realist evaluation to investigate the implementation of the National Clinical Programme for Diabetes (NCPD), a multifaceted change programme led by healthcare professionals (HCP).

Semi-structured interviews were conducted with a purposive sample of members of the national working group (n=20). Framework analysis was used to identify the underlying rationale for the programme and develop hypotheses regarding the conditions that facilitate or impede implementation. These hypotheses will be examined in using a mixed methods multiple case study design in four geographical regions (HCP, management, patients). The programme theory will be refined and cross-case comparison will examine whether the components for successful implementation differed across regions.

Given the 'black spots' and 'pockets' of good practice, the purpose of the programme is to develop 'a cohesive strategy' for resource allocation to ensure a standardised national service. Part of the underlying rationale was that establishing national clinical leadership would foster buy-in and empower frontline staff. However, implementation has been impeded by 'missed opportunities' to utilise local clinical experience. One participant suggested that the poor uptake of the national retinopathy screening programme was due in part to the lack of a clear 'connection with the clinicians on the ground'. Participants suggested there has been little change in the shared management of patients between primary and secondary care.

National stakeholders agreed on the need for and purpose of the programme. However, the lack of progress on integrated care challenges the intended outcome of a standardised diabetes service for all patients.

This study is funded by the Health Research Board Research Leader Award

P: 55

Bacterial-mediated DNA delivery to tumour associated phagocytic cells

Submitting Author: Carola Murphy

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Discipline/Area: Cork Cancer Research Centre, University College Cork

Abstract:
Phagocytic cells including macrophages, dendritic cells and neutrophils are now recognised as playing a negative role in many disease settings including cancer. In particular, macrophages are known to play a pathophysiological role in multiple diseases and present a valid and ubiquitous therapeutic target. Technology to target these phagocytic cells *in situ*, both selectively and efficiently, is required in order to translate novel therapeutic modalities into clinical reality. We present a novel delivery strategy using non-pathogenic bacteria to effect gene delivery specifically to tumour-associated phagocytic cells. Non-invasive bacteria lack the ability to actively enter host cells, except for phagocytic cells. We exploit this natural property to effect 'passive transfection' of tumour-associated phagocytic cells following direct administration of transgene-loaded bacteria to tumour regions. Using an *in vitro*-differentiated human monocyte cell line and two *in vivo* mouse models (an ovarian cancer ascites and a solid colon tumour model) proof of delivery is demonstrated with bacteria carrying reporter constructs. The results confirm that the delivery strategy is specific for phagocytic cells and that the bacterial vector itself recruits more phagocytic cells to the tumour. While proof of delivery to phagocytic cells is demonstrated *in vivo* for solid and ascites tumour models, this strategy may be applied to other settings, including non-cancer related disease.

Animal procedures were performed according to national ethical guidelines following approval by the UCC Animal Experimentation Ethics Committee.

The authors wish to acknowledge support relevant to this manuscript from Breakthrough Cancer Research, the Irish Cancer Society and the Health Research Board.

P: 56

Experiences of the use of Biosimilar Medication in Inflammatory Bowel Disease

Submitting Author: Clodagh Murphy

List of Authors: C. Murphy, K. Sugrue, G. Mohamad, J. McCarthy, M. Buckley

Discipline/Area: Centre for Gastroenterology, Mercy University Hospital, Cork, Ireland

Abstract:
A biosimilar medicine is a biological medicine that is developed to be similar to an existing reference biological medicine and have been viewed as potentially cost saving. Biosimilar infliximab, Inflectra was introduced in the department for IBD patients requiring commencement of anti-TNF treatment from January 2014.

In this descriptive study, 14 consecutive patients who were commenced on Inflectra from January to July 2014 are compared to 22 consecutive patients commenced on Remicade from Dec 2011 to Dec 2013. A direct comparison and statistical analysis was performed investigating surgery rates, readmission rates, use of steroids, disease activity and CRP trends.

Demographics of both patient cohorts were comparable. 29% of patients in Inflectra group required surgery versus 0% in the Remicade group (p= 0.02).80% of the inflectra group required hospital readmission versus 5% of the remicade group. (p=0.00004). 60% of patients in the Inflectra group needed steroid augmentation of standard steroid tapering protocol with 50% requiring multiple increases in steroid dose versus 8% of patients in the Remicade (p-value = 0.0007). Over the course of 8 weeks, 93% of patients in the Inflectra group had an increase in CRP with 7% remaining unchanged whereas 100% of patients in the Remicade group had a decrease in CRP (p=<0.001).

Our results suggest that biosimilars may not be as efficacious as the reference medicine. The results found suggest biosimilar medications will require testing in the IBD population and data cannot be ex**TRAP**olated from other disease populations.

P: 57

Automated neonatal brain volumetric analysis in Down Syndrome

Submitting Author: Keelin Murphy

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Discipline/Area:

Abstract:
This study aims to develop an automated MRI brain tissue segmentation algorithm and apply it to tissue volume analysis in neonates with Down Syndrome (DS).

Neonates with DS and healthy term controls underwent MRI. Coronal T2 scans were acquired in a 1.5T scanner. Total brain tissue (TBT) was divided into cortical grey matter, white matter, deep nuclear grey matter, brainstem and cerebellum. TBT, in addition to ventricles and extra-axial cerebrospinal fluid, formed total intra-cranial volume (TICV). Two observers annotated all seven tissues types in three slices per scan. A third observer annotated ventricles and cerebellum on every slice for 18 subjects. An automatic algorithm, using supervised learning techniques was developed to segment all tissues in every slice allowing volumes to be calculated.

Thirty neonates (20 DS, 10 controls) were recruited. Mean birth gestations and weights were: DS group: 38^{+3}wks and 3006g, control group: 39^{+1}wks and 3340g. The automated segmentations were compared with the observers' annotations using Dice-coefficient (DC). The mean (SD) DC across tissues was 0.81 (0.06). Between the two observers this was 0.86 (0.06). After adjustment for TICV, ventricular volumes are significantly larger in the DS group ($p=0.00001$) while TBT and cerebellum are significantly smaller ($p=0.02$ and $p=0.03$ respectively).

An automatic method to segment brain tissues in MRI has been developed. This demonstrated, for the first time, that ventricle, cerebellum and TBT volumes are significantly different in neonates with Down syndrome.

This work had full ethical approval and was funded by the Translational Research Access Program.

P: 58

Changes in nutritional status after minimally invasive oesophagectomy (MIO) with an enhanced recovery after surgery (ERAS) programme & aggressive nutritional intervention

Submitting Author: Éadaoin Ní Bhuachalla

List of Authors: Ní Bhuachalla É (1), Cushen S (1), Murphy T (2) and Ryan A (1)

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Discipline/Area: School of Food & Nutritional Sciences, University College Cork

Abstract:
Oesophagectomy is an exemplar of controlled major trauma associated with impaired nutritional status. Early nutritional support may limit catabolism, but its role in an ERAS protocol after major surgery is unclear. The study aimed to examine nutritional outcomes in patients presenting for MIO.

Patients were enrolled in an ERAS protocol including written education, pre-emptive analgesia, pre-op oral nutritional drinks, early mobilisation, enteral nutrition commenced on post-op day 1 and early introduction of diet. Body composition assessment, by computed tomography (CT) and multi-frequency bioelectrical impedance analysis (BIA), progression to diet and patient-reported global quality of life (QOL) scores (EORTC QLQ-C30) were prospectively collected pre-op and at 1, 3 and 6 months post-op.

A total of 47 patients (77% male) participated. The mean age, pre-op weight loss and BMI were 61years, 5.6% and 28.2kg/m^2 respectively. Only 17% had a healthy BMI, 57% were overweight and 26% obese. CT analysis found 39% to be sarcopenic pre-op. Oral diet was introduced after a median of 4 days. The median length of stay was 8 days. Weight decreased from 84kg pre-op to 80kg at 1 month and 76kg by 6 months (p=0.001). BIA found lean tissue mass (LTM) decreased from 47kg to 42kg (p=0.035) at 1 month but no significant loss occurred after that time point. Global QOL decreased at 1 month but returned to pre-op values by 3 months post-op.

An ERAS protocol is associated with early discharge and assists in post-op recovery. There is a significant decline in nutritional status post MIO, particularly LTM, however this stabilises at 1 month after which time QOL scores return to baseline.

This research was funded by the Health Research Board and Abbott Nutrition.

P: 59

Potential therapeutic gain in stereotactic radiosurgery of cerebral arteriovenous malformations by radiation dose enhancement with gold nanoparticles

Submitting Author: Aiman Nor

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Discipline/Area: Department of Radiation Oncology, University College Cork, Cork

Abstract:
Cerebral arteriovenous malformations (AVM) occur worldwide in all population groups and have universal annual hemorrhagic rates of 3%. Hemorrhagic events (strokes) are the most common source for morbidity and mortality. Stereotactic radiation is a well-established therapeutic option, but the outcome is influenced by the AVM volume, its location, and the radiation dose. Only complete obliteration is considered a cure, but this can be difficult to achieve for complex shaped AVMs with present radiosurgical techniques.
The radiation dose enhancement resulting from the irradiation of gold nanoparticles with photons was researched in the literature (1,2) as was the role of angiogenesis and its regulation via vascular endothelial growth factors and their cell membrane receptors (3).
To improve on the results the use of intra lesion deposited, radiation dose enhancing gold nanoparticles (AuNP) is proposed. The primary target in AVM radiosurgery are the endothelial cells, whose cell death triggers the cascade of events that lead to obliteration. Gold is very biocompatible and a radiation enhancer due to its high Z. The interaction with photons generates much localized secondary radiation energetic enough to cover the entire content of the endothelial cells. Linking the AuNP to a membrane receptor antibody makes selective AVM endothelial cell adherence possible, because human brain AVM endothelial cells express VEGFR2 differently than normal brain blood vessels. Such antibody complexes create an intracellular dose enhancement when the AuNP is irradiated.
The proposed approach allows for localized radiation enhancement, thereby theoretically improving obliteration rates and shortening
the latent times.

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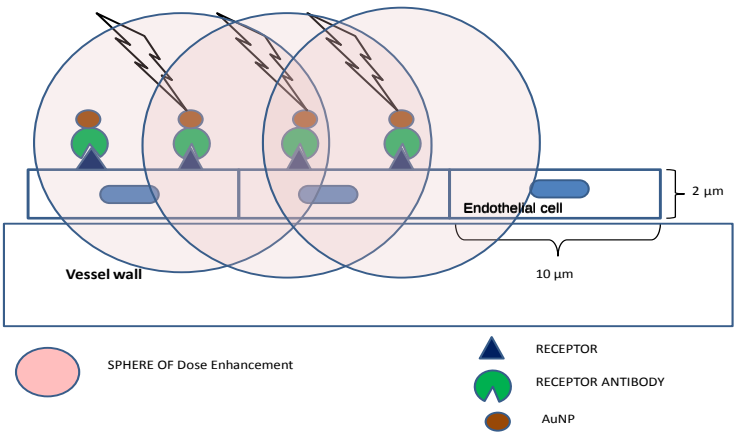

P: 60

The nuclear receptor TLX regulates motor, cognitive and anxiety-related behaviours during adolescence and adulthood

Submitting Author: James O'Leary

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Discipline/Area: Department of Anatomy and Neuroscience, University College Cork

Abstract:
Adolescence is a critical period for postnatal brain maturation and susceptibility to emotional and cognitive-related disorders. Mice lacking the nuclear receptor Nr2e1 (TLX) display deficits in adult hippocampal neurogenesis and exhibit some behavioural abnormalities. However, the role of TLX in cognitive, anxiety and motor behaviours during adolescence remains unexplored. Moreover, whether behavioural deficits are sex-dependent has not yet been investigated. Thus, the aim of this study was to determine the role of TLX in cognitive, anxiety and motor behaviours in adolescent male and female mice with a spontaneous deletion of the TLX gene ($Nr2e1^{-/-}$). Results indicate that adolescent male and female $Nr2e1^{-/-}$ mice were hyperactive in a novel environment, and this effect persisted into adulthood. Furthermore, male $Nr2e1^{-/-}$ mice exhibited a reduction in open field thigmotaxis during adolescence and adulthood, suggesting that TLX might modulate anxiety-like behaviour. Spontaneous alternation, a hippocampal-dependant working memory task, was impaired in adolescent but not adult male and female $Nr2e1^{-/-}$ mice. Similarly, contextual fear conditioning (a hippocampal-dependent cognitive task) was impaired in male adolescent $Nr2e1^{-/-}$ mice, but this effect did not persist into adulthood. $Nr2e1^{-/-}$ adolescent male and female mice showed impaired cued fear conditioning (a hippocampal-amygdala dependent cognitive task) and this deficit persisted in adult male $Nr2e1^{-/-}$ mice only. Together, these findings suggest that TLX plays a key role in cognitive and anxiety-like behaviours during adolescence and in motor activity during adolescence and adulthood. Moreover, some of these effects are sex-dependent.

All experiments were conducted in accordance with the European Directive 2010/63/EU, and under an authorization issued by the Health Products Regulatory Authority Ireland and approved by the Animal Ethics Committee of University College Cork.
This work was supported by Science Foundation Ireland (SFI/IA/1537).

P: 61

The Association of Night-Time Systolic Blood Pressure with Ultrasound Markers of Subclinical cardiac and Vascular Damage

Submitting Author: Anne Marie O'Flynn

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Discipline/Area: Department of Epidemiology and Public Health, University College Cork

Abstract:
Introduction: Our aim is to examine the association of night-time systolic blood pressure (SBP) with left ventricular systolic dysfunction measured by global longitudinal strain (GLS) and carotid intima media thickness (CIMT) and carotid plaques.

Methods: This is a substudy of the Mitchelstown Cohort Study. The Clinical Research Ethics Committee of the Cork Teaching Hospitals provided ethical approval. In 2014 participants were invited to have repeat ambulatory blood pressure monitoring, echocardiogram and carotid ultrasound. GLS was measured by speckle-tracking analysis of echocardiographic images. Normal cut-off was -19.7%.[(1)] Mean CIMT was measured from still images taken from 3 angles on both sides. Normal cut-off was the 75th percentile. [(2)] The presence of carotid plaques was recorded. Philips QLAB cardiac and vascular ultrasound quantification software was used for analysis. Logistic regression assessed the association of night-time SBP with GLS, CIMT and carotid plaques.

Results: Fifty participated in the present study. Mean GLS was -21.2% and mean CIMT was 0.72mm. Thirty-three (66%) had carotid plaques. In univaribale analysis baseline night-time SBP was significantly associated with abnormal GLS (OR 1.9 for every 10mmHg rise, 95% CI 1.1 – 3.2) and carotid plaques (OR 1.9 for every 10mmHg rise, 95% CI 1.1 – 3.2). No significant associations were found for daytime SBP. In multivariable models including sex, age and daytime SBP associations for night-time SBP were no longer statistically significant.

Conclusion: Night-time SBP appears to be associated with abnormal GLS and the presence of carotid plaques. These findings need to be reproduced in a larger prospective study incorporating chronotherapy.

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Funding:
Dr Anne Marie O'Flynn is funded by a Health Research Board Research Training Fellowship (reference HPF/2012/14) and has also received the Irish Heart Foundation John Feely research bursary to support this work.

P: 62

Molecular Diversity in the Hepatitis C Virus

Submitting Author: Peter Anthony O'Callaghan

List of Authors: O'Callaghan PA, Palmer BA, Fanning LJ.

Discipline/Area: Department of Medicine, University College Cork

Abstract:
Introduction: Hepatitis C is a virus with a large genetic diversity. The highest variability is seen in the HVR1 region within the E1E2 genes. The E1E2 glycoprotein plays an important role in the evasion of the host immune response. The large degree of molecular heterogeneity can aid in our understanding of the phylogeography of the virus.

Aim: To identify the most likely genotype of 10 anonymised samples by comparing their nucleotide sequence against a reference database. To illustrate the genetic variability via phylogenic analysis. To perform a global nearest neighbour phylogeographic analysis.

Methods: Serum samples were obtained from an unselected group of 10 HCV positive. The samples were sequenced using standard Sanger Dideoxy methods. Using pairwise alignment nucleotide sequences were screened against a HCV database of globally representative sequences.Phylogenetic analysis was performed using MEGA 6 software. Phylogeographic analysis was performed using curated data from the HCV lanl database.

Results: Out of the 10 samples sequenced, three samples were identified as Genotype 1a, one as 1b, one as 2b, two as 3, one as 3a, and one as a putative 6i. One sample was recalcitrant to DNA sequencing for undefined reasons. The closest matched sequences exhibited a wide geographical distribution.

Conclusion: This small sample pool reflected the large genetic and global diversity known to exist for the hepatitis C virus. We present data on the viral heterogeneity and phylogeography of this sample set.

Funded through the School of Medicine's Supplemental Award.

P: 63

Calculating the Impact of Population-level Implementation of the LEAP Protocol to Prevent Peanut Allergy

Submitting Author: Cathal O'Connor

List of Authors: O'Connor C, Kelleher M, Hourihane JO'B.

Discipline/Area: Department of Paediatrics, UCC, Cork

Abstract:
The recently published LEAP study showed early introduction of peanut led to a substantial reduction in the incidence of peanut allergy in a highly selected group of children at increased risk of peanut allergy. We have modelled the impact of implementation of the LEAP study protocol and outcomes at a national population level in Ireland.

We used the data from the LEAP study and its published outcomes (Intention to treat with worst case imputation), Irish national birth statistics and data from the BASELINE birth cohort study regarding atopic dermatitis prevalence and severity at 6 months, food sensitisation at 12 months and peanut allergy at 2 years.

68,684 children were born in Ireland in 2013. With a prevalence of peanut allergy of 1.75%, the projected number of cases of peanut allergy in these children is 1, 202. Successful replication of LEAP protocols in Ireland would decrease the number of estimated new cases of peanut allergy in 2,932 LEAP-eligible children from 480 to 140 (a relative reduction of 71%). This only represents an absolute reduction of 29% in all cases of peanut allergy from 1202 to 852 per annum.

More cases of peanut allergy occur in children not considered eligible for LEAP than in LEAP-eligible children, so other, simpler approaches need to be developed to further reduce the incidence of peanut allergy.

Funding: None.
The BASELINE cohort is supported by the National Children's Research Centre, Dublin, Ireland and by the Food Standards Agency, United Kingdom (TO7060).

P: 64

Detecting Diabetes Mellitus and Prediabetes in patients with acute stroke

Submitting Author: Antoinette O'Connor

List of Authors: O'Connor A (1), Hannon E (2), Murphy O (1), Harnedy N (2), Cronin S (1)

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(2) Department of Geriatrics, Cork University Hospital

Discipline/Area: Department of Neurology, Cork University Hospital

Abstract:
Stroke is a leading cause of death and disability[1]. Control of modifiable risk factors is the most effective approach to decreasing the burden of stroke[2-4]. The purpose of this study was to determine the prevalence of diabetes mellitus (DM) and prediabetes (pre-DM) in acute stroke patients in an Irish population.

We conducted a retrospective review of the records of stroke patients admitted to Cork University Hospital from 9th March 2014 to 9th March 2015. HbA1C and fasting glucose measurements during admission were recorded. DM and pre-DM prevalence levels were determined using both HbA1C and fasting glucose level.

Among 445 strokes admitted to CUH, 383 (86%) had a test for diabetes performed. 241 (54%) had a HbA1c check, while 252 (57%) had a measurement of fasting glucose performed. 39 (9%) had a HbA1c level > 47mmol/l. 40 (9%) had a HbA1c between 42-47 mmol/l. 27 (6%) had a fasting glucose greater than 7mmol/l. The rate of Impaired Fasting Glucose varied from 7 - 21% dependant on range used.

In our study 6-9% of acute strokes had either a fasting glucose or HbA1c consistent with DM, while 7-21% had pre-DM. The rate of detection of DM and pre-DM varies with diagnostic test performed, suggesting that both HbA1c and fasting glucose should be performed in cases of acute stroke.

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P: 65

Should the use of the Extended Myositis Antibody (EMA) panel be part of the routine work-up in suspected myositis?

Submitting Author: Antoinette O'Connor

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Discipline/Area: Department of Neurology, Cork University Hospital

Abstract:
The approach to diagnosis and management of inflammatory myopathies has evolved [1]. More precise molecular diagnosis is now possible leading to improved phenotyping and targeted therapies[1]. Myositis can present to a myriad of specialties necessitating a cohesive and collaborative approach. The objective of this study was to determine the clinical utility and cost effectiveness of the Extended Myositis Antibody (EMA) panel in suspected immune myopathy.

Records of all EMA panels from April 2014 -Mar 2015 were reviewed. EMA assay was performed at University Hospital Galway using Euroline Immune Assay. Patient charts were interrogated for clinical details, treatments and outcomes. Results of additional investigations (EMG, MRI, muscle biopsy) were documented.

22 patients (mean age:55, SD:15) had an EMA panel sent during the study period. Neurology (n=4, 18%), Rheumatology (n=5, 23%), Respiratory (n=8, 36%) and Other (n=5, 23%) specialties requested the test. A positive EMA panel was identified in n=6 (27%) providing vital diagnostic and prognostic information. Ten (46%) had other positive autoantibodies. Additional investigations performed included cardiac or musculoskeletal MRI (n=8, 36%) and muscle biopsy (n=6, 27%).

The EMA panel is invaluable in defining a heterogeneous patient population into clinicoserological phenotypes, thus supporting its routine use in suspected myositis.

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P: 66

Enhanced Autophagy – an effective treatment for drug resistant cancers

Submitting Author: Tracey O'Donovan

List of Authors: O'Donovan, T., Rajendran, S., El-Mashed, S., O'Sullivan, GC., McKenna, SL.

Discipline/Area: Cork Cancer Research Centre, University College Cork

Abstract:
Effective chemotherapy regimens must induce programmed cell death (PCD) in cancer cells. While apoptosis is regarded as the central mediator of PCD, it is often defective in cancer cells. We have previously shown that oesophageal cancer cells treated with chemotherapeutics, respond by inducing autophagy and recover following drug withdrawal. Knockdown of autophagy regulators Beclin1 and Atg7 with siRNA, enhanced the effect of 5-fluorouracil (5-FU) and reduced this recovery (1). Here, we propose that an alternative strategy to improve chemotherapeutic efficacy is to combine autophagy inducers with chemotherapy, thus inducing excessive autophagy and Type II cell death.

The effects of combination treatment were assessed *in vitro* using morphology and colony formation assay. Treatment outcomes in murine models of localised and metastatic tumours were measured using bioluminescent imaging and analysis of tumour volume and lung weights.

In vitro, we have shown that augmentation of autophagic/Type II cell death significantly reduces the recovery of cancer cells following withdrawal of chemotherapeutic drugs, 5-FU and cisplatin. *In vivo,* implementation of this approach has shown success in preclinical models of lung, breast and colorectal carcinoma (2). Combinations of an autophagy inducer and 5-FU or oxaliplatin have effectively reduced both primary and secondary tumour burden, with improved survival. Histological analysis has demonstrated that the principal mechanism of cell death is Type II cell death, with enhanced levels of autophagy.

This treatment protocol offers a new strategy to eliminate drug resistant, apoptotic incompetent cancer cells and reduce metastatic disease by the eradication of primary and disseminated tumour cells.

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P: 67

Long, non-coding RNAs in breast cancer: analysis of lncRNA patient profiles to influence experimental design of a tethered RNA system

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Discipline/Area: School of Medicine, University College Cork

Abstract:
Within the past decade, it has become clear that the human genome is largely transcribed, but only a small percentage of the transcriptome codes for proteins (1). In particular there has been the emergence of long, non-coding RNAs (lncRNAs; >200 nucleotides in length) as regulators of normal cellular events and various disease states, including breast cancer (2). Although lncRNAs are still being discovered, there is a particular lack of information regarding the biological roles and the molecular interaction partners of lncRNAs that have been identified.

To address the biological roles of lncRNAs, we would like to pioneer the use of a tethered RNA system (3) to uncover lncRNA-binding proteins. In order to make an informed decision for our experimental design, we have further analysed lncRNAs identified as a prognostic signature of metastatic breast cancer in patients by Sorensen et al. (4) for suitability in our tethered RNA system. Using overall and estrogen-receptor positive (ER+) lncRNA profiles (4), additional information to each lncRNA entry was added using Ensembl (5) and LNCipedia (6). This includes alternative gene names, disease and clinical information, total number of transcripts and number of transcripts with lengths under 1,000 nucleotides, along with "strand" (sense/antisense) information. Compilation of information on breast cancer-associated lncRNAs into a workable database has been an important first step for helping us determine the most appropriate lncRNAs for our experimental system.

The authors gratefully acknowledge funding from the Medical Research Supplement Award, School of Medicine, University College Cork, to progress this project.

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P: 68

IL-IB negatively impacts upon expression of both inflamattory and neurogensis - associated signalling molecules in hippocampal neural stem Cells in vitro

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Discipline/Area: Department of Anatomy and Neuroscience, University College Cork

Abstract:
Hippocampal neurogenesis, the process by which new neurons are produced, has been shown to be involved in some forms of memory and emotion regulation. IL-1β, a key mediator of neuroinflammation within the brain, has been shown suppress proliferation of neural stem cells (NSCs). TLX is an orphan nuclear receptor known to regulate the proliferation of NSCs. IL-1β is shown to negatively impact upon TLX expression in proliferating NSCs. We aim to elucidate the mechanisms of how IL-1β signalling interacts with TLX. We prepared embryonic day (E)18 hippocampal neurosphere cultures from rats (Ethical Approval No:2013/027), and examined the effects of IL-1β on gene and protein expression of p65 (a downstream signalling effector of IL-1β, TLX and associated co-signalling molecules). IL-1β impaired neurosphere growth after incubation for 3 days in vitro (DIV). We established that p65 signalling is activated within 10 minutes of stimulation with IL-1β. We also show a negative feedback mechanism is evident after 30 minutes of IL-1β exposure as shown by increased IκBα expression, a negative inhibitor of p65 signalling. There was no effect of IL-1β on the p65 co-signalling molecule Creb Binding Protein (CBP). We show that IL-1β suppressed TLX and its co-signalling molecule HDAC5 in a time dependent manner. This study establishes a time-course of IL-1β-induced changes on both an inflammatory signalling mediator and a regulator of neurogenesis in hippocampal NSCs *in vitro,* and proposes therapeutic target points that may be exploited to mitigate the negative effects of IL-1β on hippocampal neurogenesis and associated cognition.

P: 69

Screening for delirium with the Six-item Cognitive Impairment Test

Submitting Author: Niamh O'Regan

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Discipline/Area: Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork

Abstract:
Delirium is highly prevalent, though remains under-diagnosed. This study aimed to assess the diagnostic accuracy of several bedside cognitive tests in screening for prevalent delirium in older medical inpatients.

Participants were assessed within 36 hours of admission using the Delirium Rating Scale-Revised '98 (DRS-R98), as well as the 6CIT (Six-item Cognitive Impairment Test); the clock-drawing test; overlapping pentagons; months of the year backwards; spatial span forwards; and a verbal test of visuospatial function. Chi-square statistic; Receiver Operating Curves; and sensitivities and specificities with 95% confidence intervals were used to estimate diagnostic accuracy with DRS-R98 diagnosis as the reference standard. Discriminant analysis investigated how the screening tests differentiated delirium from dementia without delirium and from normal controls. The study was funded by the Health Research Board. Ethical approval was granted by the local research ethics committee.

Of 555 patients approached, 470 had full delirium assessments performed (median age 81 years; 50.3% female). Prevalent delirium on admission was diagnosed in 184 patients. In screening for delirium, the most robust test was the 6CIT with an AUC of 0.87 (95% CI 0.84-0.91). Additionally, on discriminant analysis**,** only the 6CIT significantly differentiated subjects with delirium from those with dementia but no delirium, and from normal controls (Wilks Lambda=0.748, F=62.15, df1:1, df2:1, df3:184, $p<0.001$).

The 6CIT incorporates quick tests of orientation, attention and logical memory, all commonly affected in delirium. Our results indicate that this test may facilitate screening for prevalent delirium in older medical inpatients and help to differentiate delirium from dementia on admission.

P: 70

Pre-delirium Features Predict Delirium Onset

Submitting Author: Niamh O'Regan

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Discipline/Area: Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork

Abstract:
Delirium is a serious and prevalent condition in hospitals. Identification of a delirium prodrome could promote earlier detection and management. Our aim was to identify prodromal features of delirium in older medical inpatients.

Medical inpatients of ≥70 years were assessed within 36 hours of admission using the Delirium Rating Scale-Revised '98 (DRS-R98). Consenting subjects without prevalent delirium were then assessed daily for delirium development. Proportional Hazards models analysed the development of prodromal features prior to the development of incident delirium. In this study the prodromal features of interest were DRS-R98 items which became positive prior to the onset of delirium. Formal ethical approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. This study was funded by the Health Research Board.

Of 555 approached, 191 were included (mean age 80 years, 52.9% male), and 61 patients developed delirium. Controlling for confounders, we found that positive scores on several DRS-R98 items were significantly predictive of imminent delirium. These included sleep-wake cycle disturbance (Hazard Ratio (HR) 1.48, 95% CI 1.08-2.04, p=0.016); perceptual disturbances and hallucinations (HR 1.1, 95% CI 1.03-1.17, p=0.006); lability of affect (HR 1.14, 95% CI 1.05-1.24, p=0.002); attention (HR 1.32, 95% CI 1.23-1.42, p<0.001); short-term memory (HR 1.45, 95% CI 1.18-1.78, p<0.001); temporal onset of symptoms (HR 1.34, 95% CI 1.22-1.47, p<0.001); and fluctuation of symptom severity (HR 1.27, 95% CI 1.09-1.48, p=0.002).

Prodromal delirium features were significantly associated with progression to delirium in older medical inpatients. Recognising these features may facilitate earlier detection.

P: 71

Can the NICE delirium screening criteria detect delirium?

Submitting Author: Niamh O'Regan

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Discipline/Area: Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork

Abstract:
Delirium is highly prevalent, yet diagnosis is challenging. In 2010, NICE Guidelines for the Diagnosis, Prevention and Management of Delirium recommended that all at risk inpatients should be screened daily by monitoring for changes in cognitive function; physical function; perception; and social behaviour (1). This process has not yet been validated, hence our aim was to assess its efficacy in the clinical setting.

Older medical inpatients were assessed using the Confusion Assessment Method (CAM) and the Delirium Rating Scale-Revised '98 (DRS-R98) by an experienced rater. Relevant nursing staff were surveyed by blinded independent researchers using a novel questionnaire based on the NICE recommendations. Discriminant analysis was used to identify which aspects could distinguish patients with delirium from those without. This study was funded by the Health Research Board and ethical approval was granted by the local research ethics committee.

Seventy patients had dual assessments: 9 had delirium defined using DRS-R98, and 14 using CAM. Twenty-nine patients (41.4%) screened positive using the NICE-based questionnaire. The only domain in which changes significantly predicted delirium / not delirium group classification was 'cognitive change': using CAM 82.9% were correctly classified (sensitivity 0.42, 95% CI 0.17-0.71; specificity 0.93, 95% CI 0.82-0.98) and using DRS-R98 77.1% were correctly classified (sensitivity 0.25, 95% CI 0.04-0.64; specificity 0.85, 95% CI 0.73-0.93).

Screening tests, particularly as part of a two-step diagnostic approach, should favour sensitivity over specificity to avoid missing cases. This work suggests that operationalised NICE recommendations are too specific to be useful as a screening test.

1. Delirium: Diagnosis, prevention and management. London: National Institute for Health and Clinical Excellence, 2010.

P: 72

The Role of Communication between Health Professionals and Patients as a Factor in Patient Complaints in Obstetrics- a Mixed Methods Review from an Irish Maternity Hospital

Submitting Author: Sinead O Reilly

List of Authors: Sinead O Reilly (Medical Student UCC, Cork), Sarah Meaney (National Perinatal Epidemiology Centre, UCC, Cork), Anne Marie Kenny (Quality and Safety Office, CUMH, Cork), Mairead O Riordan (Consultant Obstetrician/Clinical Lead in Quality and Safety UCC/CUMH Cork)

Discipline/Area: Medical Student, University College Cork

Abstract:
The purpose of the research was to explore the role of staff communication with patients and how this impacted on patient's decision to submit a complaint.

There were 17,000 births and 113 complaint letters in Cork University Maternity Hospital over a two year period. Letters were analysed using a mixed methods approach; key quantitative data was obtained and then letters were reviewed using thematic analysis.

In 93% of letters staff communication was cited as a significant issue by patients, in 56% of letters more than one communication issue was raised. Patient's focus of complaint was often on communication rather than clinical outcome. Most complaints focused on Emergency Room and Labour Ward. 46% of all clinical obstetric complaints were by mothers experiencing a first pregnancy/delivery. Complaints against medical staff were often around a lack of communication while complaints against midwifery staff were around issues of trust. Three key themes emerged; patients sense of a loss of autonomy during delivery, impact of pregnancy loss on parents and staff communication during this time and patients have high expectations of obstetric care and the psychological implications can be profound when this was not achieved.

Patients often judge their experience of care on the communication skills of clinical staff that they interact with. Women's expectations of delivery are high and disappointment occurs when these expectations are not achieved. Communication skills during high-stress situations can be an important trigger for a complaint and one which staff need support around particularly in the Labour Ward and Emergency Room.

P: 73

Northern Ireland Audit of Dementia Care in Acute Hospitals

Submitting Author: Emma O'Shea

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Discipline/Area: Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork

Abstract:
Introduction: Hospital admission is associated with adverse outcomes, including increased mortality, and functional and cognitive decline in people with dementia, calling into question care quality. This audit aimed to assess the baseline quality of dementia care in acute hospitals in Northern Ireland.

Methods: Data was collected on multidisciplinary assessment, antipsychotic prescription and use, access to specialist services, staffing levels, staff training, and discharge planning, through case-note review (n=240), and interviews with clinicians and hospital- and ward-level management across 12 hospitals.

Results: Physical assessment was good generally however mobility, pain and functional assessments were under-performed. Cognitive (33%) and delirium (30%) assessment was suboptimal; less than half of patients had collateral history recorded. Few patients (8%) were prescribed antipsychotics de novo, most commonly for "agitation" (55%). Psychology services were unavailable to most wards. No hospital had mandatory dementia training. Discharge planning was initiated within 24 hours of admission for 16% of patients.

Conclusion: Deficits in dementia care were identified; improvements are required in these areas, as the demand for acute dementia care grows in the population. Work streams are currently in development to implement the recommendations of the audit, in line with the Northern Ireland Regional Dementia Strategy.

Funding for this audit was provided by Atlantic Philanthropies.

P: 74

Basehunter - a bacterial based DNA detection

Submitting Author: Donnchadh O'Sullivan

List of Authors: Donnchadh O'Sullivan, Aoife O'Brien Horgan, Amy Keane, Brandon Malone, Leanne O'Sullivan, Shama Chilakwad, Timothy O'Flynn, Dr. Paul Young, Prof. Tommie Mc Carthy

Discipline/Area: School of Biochemistry and Cell Biology, University College Cork.

Abstract:
Our project is a novel bacterial method of DNA detection. We have developed a customisable, linearised, double stranded plasmid with two sticky overhangs. When the sticky overhangs come into contact with a target sequence, the binding of the DNA sequence to the overhangs circularises the plasmid. The circularised plasmid is then transformed into competent E. coli cells. Bacterial growth of green fluorescent colonies indicates a positive result, therefore the complementary DNA target sequence was present. This system could act as a cheap alternative to both digital and real time PCR, as target DNA fragments are amplified in living cells without the use of a costly PCR machine. This system could potentially be used as a diagnostic or screening tool for viral and/or bacterial infection such as Human Papilloma Virus, Mycobacterium tuberculosis. By improving sensitivity and specificity this system could also be used for the detection of genetic mutations resulting in disease such as cystic fibrosis.

P: 75

The sound of silence: analysis of invariant and synonymous codon sites across the E1/E2 gene junction in Hepatitis C virus

Submitting Author: Brendan A. Palmer

List of Authors: Brendan A. Palmer and Liam J. Fanning

Discipline/Area: Molecular Virology Diagnostic & Research Laboratory, Department of Medicine, University College Cork

Abstract:
Hepatitis C virus (HCV) is a positive-sense single-stranded RNA virus. The HCV genome displays considerable diversity, contributed to in part by the accommodation of hypervariable regions (HVR) in the E2 spike glycoprotein. Nonsynonymous change at HVR1 over time averts epitope recognition and contributes to immune escape. We have previously interrogated the temporal dominance of HCV lineages within a treatment naïve patient, over a decade of chronic infection using ultradeep pyrosequencing and reported a virome progressing from a complex, mixed lineage quasispecies to a low diversity, single lineage population of equivalent fitness (1).

In the current study we explore the underlying invariant and synonymous codon usage patterns in the context of lineage exploration of sequence space. We document lineage specific evidence of synonymous epistatic co-evolution across the E1/E2 gene junction. Where present, the majority of sites were found together as networks of synonymous co-evolution. Such events were coincident with lineage frequency fluctuations to the virome, HVR1 epitope change and humoral immune activity. Conversely, limited co-evolution between sites was recorded for the surviving, low diversity, lineage within which the dominant HVR1 was stably maintained longitudinally over time.

Overall, our observations identify synonymous mutation as an indicator of viral fitness. Co-evolution at multiple synonymous sites was concomitant with HVR1 epitope change. The absence of co-evolving networks occurred where the dominant HVR1 was stably maintained. For this latter lineage of low diversity, evolution of the sequence is on-going, but in a manner that minimises mutational risk and maximises variant fitness.

1. Palmer BA. et al., J. Virol. 2014; 88: 13709 - 13721.

P: 76

Can gene sequencing identify additional genetic variants predicting for 5-Fluorouracil toxicity? - A cohort of Irish patients

Submitting Author: Aine Peoples

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(2) University College Cork
(3) Companion Dx, Houston TX

Discipline/Area: University College Cork

Abstract:
Introduction: Fluoropyrimidine chemotherapy drugs are used in the treatment of a variety of malignancies. A substantial minority of patients develop severe toxicities with these agents. Previously identified genetic variants can predict toxicity in some, but not all patients. This study aimed to identify further predictors for toxicity by using targeted gene sequencing of genes involved in fluoropyrimidine metabolism.

Methods: Ethical approval was obtained through the Cork Research Ethics Committee of the Cork Teaching Hospitals (CREC). Patients treated with 5-FU based chemotherapy for colorectal cancer in the Bons Secours Hospital, Cork between 01/01/2012 - 06/06/2015 and who had prophylactic DPYD testing were eligible if they had previously tested wild type for 4 known mutations in the DPYD gene - a gene involved in fluoropyrimidine metabolism. Those who experienced grade 3/4 toxicity are the case population and those who did not have severe toxicity are the control population. Buccal swabs were taken to obtain DNA samples and subsequently sent for genotyping to a collaborating laboratory in the USA. (CompanionDx, TX) First pass analysis will check again for the commonest DPYD mutations and for less common polymorphisms in DPYD and TYMS. Cases with no known polymorphisms to explain toxicity will have deep sequencing performed.

Results: We recruited 20 cases and 29 controls. Results are pending. Genotyping is in progress. Cost of testing circulating WBC for 4 commonest mutations is approximately 100 euro and cost of expanded panel (includes these) is only slightly more.

Discussion & Conclusion: It is more cost effective to carry out prospective testing when compared to the cost of hospital admission and stay following grade 3/4 toxicity. Prospective testing also incorporates a patient-centered approach to care and treatment, decreasing the number hospital admissions, decreasing patient suffering and moving one step closer to personalised medicine. It is hoped from this study that individuals who have genomic variants predisposing them to toxicity, and which would subsequently lead to hospital admission, can be easily identified in the future.

References:
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P: 77

Community-based approach to food allergy management. A case of a trans-disciplinary study in the UK and Ireland.

Submitting Author: Katarzyna Pyrz

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(1) School of Applied Psychology, University College Cork
(2) Clinical Investigation Unit, University Hospital of South Manchester
(3) Departments of Paediatrics and Child Health, University College Cork
(4) University of Manchester

Discipline/Area: School of Applied Psychology, University College Cork

Abstract:
Food allergic incidents can be life-threatening yet remain under-researched (1). Life reporting is not available for patients and bio-psychosocial co-factors are poorly understood. The *Allergic Reactions in the Social Contexts (AlleRiSC)* study has developed an online reporting tool. Measures of risk propensity and health-related quality of life are also investigated. The first datasets from this community-based prospective study inform further investigation within an EU-funded project called *iFAAM (Integrated Approaches to Food Allergen and Allergy Risk Management).*

A mixed-method design is used. The reporting questionnaire has been developed and validated in English with assistance of patients' groups. Currently, adults participants based in the UK and Ireland (N=107) report food-allergic incidents in real-time, submitting photos of symptoms and samples of culprit food. The next stage will involve rolling-out the reporting system to other European countries and cross-cultural validation.

Collected data suggest trends in the distribution of participants' sex (F=65%), age (M=33), co-morbidity (85%) and in diagnoses of food allergies (Nuts family =51%). Twenty incidents in the UK and ten incidents in Ireland got reported and six food samples collected between 04.11.2014 and 18.10.2015. The reported levels of risk propensity and the quality of life suggest significant gender and age differences.

Building on e-Health and trans-disciplinary research frameworks this study demonstrates potential to capture and explore the complexity of the population-based data. It may provide novel findings allowing for new understanding of the prevalence and psychosocial factors of food-allergic incidents. Such findings will have implications for food allergy management across Europe (2).
AlleRiSC study obtained an approval of the Clinical Research Ethics Committee in Cork on 19th June 2014.

This study is funded by the European Union within the 7th Framework Programme (ID: KBBE.2012.2.4-04)

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2. Pyrz, K., Semic-Jusufagic, A., Munro, Ch., Mills, C., Simpsons, A., Hourihane, J.O'B. & DunnGalvin, A. (2015). *How can we get better at managing food allergies in the community?* Conference Paper, An Annual Congress of the European Academy of Allergy and Clinical Immunology (EAACI), Barcelona.

P: 78

An audit of Liver Biopsies performed at the Department of Hepatology, Cork University Hospital

Submitting Author: Navneet Ramlaul

List of Authors: Ramlaul N, McCarthy K, Crosbie O.

Discipline/Area: Department of Hepatology, Cork University Hospital

Abstract:
Introduction: The aim of this audit was to ascertain the main indications for performing elective day case liver biopsies at our department and compare the findings to a similar audit performed eight years previously, prior to the routine use of Fibroscan.

Aims & Background: A previous audit in 2008 over an 18 month period revealed that most elective liver biopsies carried out in our department were to assess patients with hepatitis C prior to making a decision with regard to the need for antiviral therapy. We wanted to see if there has been a change in practice over this 7 year period.

Method: This is a retrospective study of elective day case liver biopsies performed between January 2014 and April 2015. This excluded patients who were referred to us for care and had a biopsy performed elsewhere or patients having inpatient liver biopsies.

Results: 56 elective liver biopsies were performed over a 16 month period (35 female, 21 male), mean age of patients was 50.9 years (range 14 – 78). The commonest indications for proceeding to liver biopsy were to assess and/or diagnose autoimmune hepatitis, steatosis and steatohepatitis, overlap syndromes, the cause of persistent cholestasis and hepatitis C. In 2007-2008, 34% of liver biopsies were performed on patients with hepatitis C whereas now this accounts for only 2 (3.6 %) of the total number. An overwhelming majority of biopsies now performed 29 (51.8%) were to assess autoimmune hepatitis of which 76% were females. The rest of the biopsies showed PBC/overlap syndrome 5 (8.9%), steatosis/steatohepatitis 9 (16.1%), drug induced liver injury 2 (3.6%), chronic hepatitis non-specific 5 (8.9%), cholangitis 2 (3.6%), tumour 1 (1.8%) and normal 1 (1.8%).

Conclusion: This audit clearly illustrates that since the introduction of the Fibroscan, there is rarely a need to perform liver biopsy for the assessment of hepatitis C and thus biopsies were mainly performed to diagnose and assess other conditions which would be more difficult to characterise otherwise.

P: 79

Bacteria in Patient Tumours: What, Where & How?

Submitting Author: Elizabeth Rettedal

List of Authors: Elizabeth Rettedal (1), Joanne Cummins (1), Carola Murphy (1), Deirdre O'Hanlon (2), Mark Tangney (1)

(1) Cork Cancer Research Centre, University College Cork
(2) Cork University Hospital

Discipline/Area: Cork Cancer Research Centre, University College Cork

Abstract:
The human body is home to a large and diverse population of bacteria with properties that are both harmful and beneficial to our health. The human microbiome differs from one individual to another, with the majority of available information confined to 'tract'-related body regions. However, sites once thought of as sterile, such as the stomach, bladder, lungs and placenta, are recently being shown to harbour an endogenous microbiota.

Bacteria have been linked with various cancers in a number of ways (1). For decades, bacteria of different types have been isolated from patient tumours of various organs. Recently, we and others have characterised the bacterial populations naturally present within malignant and non-malignant tissue of the breast, and reported the presence of a wide range of bacteria that varies between individuals and tumours (2). While bacterial presence in certain tumours is associated with tumourigenesis, in many cases bacterial presence may reflect selective replication of bacteria within tumours. Since it is becoming apparent that bacteria exist in some tumours, this study seeks to establish what tumours have what bacteria, and what influence on tumour initiation, progression or treatment they may have.

The authors wish to acknowledge support relevant to this manuscript from the APC Microbiome Institute, the Health Research Board and Breakthrough Cancer Research.

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P: 80

Probiotic Bacterial Trafficking To Tumours In Cancer Patients

Submitting Author: Elizabeth Rettedal

List of Authors: Elizabeth Rettedal (1), Carola Murphy (1), Michelle Cronin (1), Paul Sweeney (2), Kishore Dodukula (3), Mark Tangney (1)

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(2) Mercy University Hospital
(3) Cork University Hospital

Discipline/Area: Cork Cancer Research Centre, University College Cork

Abstract:
The phenomenon of bacterial replication specifically within tumours following intravenous administration has been known for several decades. Our research has shown that oral administration of non-pathogenic bacteria to mice results in trafficking from the Gastro-Intestinal Tract (GIT) with subsequent homing to and replication specifically in distal subcutaneous tumours (1). Sampling from humans has indicated that trafficking of non-pathogenic bacteria from the GIT (bacterial translocation) may be a phenomenon that occurs in healthy individuals and may be a normal physiological event without deleterious consequences. Numerous GIT-associated bacterial species have been isolated from infected lesions in patients. Tumour-bearing hosts present a unique model for the study of commensal bacterial translocation. It is likely that bacteria egress from the GIT at very low numbers, and are normally quickly eliminated by the immune system. However, the phenomenon of bacterial replication within tumours results in dramatic increases in bacterial numbers within a confined region, permitting an 'amplified read-out' system.

A clinical study is ongoing involving ingestion of established, commercially available probiotic bacterial suspensions (food supplements), by cancer patients of the Mercy University Hospital and Cork University Hospital. Surgical patients diagnosed with renal, lung or hepatobiliary cancers scheduled for tumour resection ingest probiotics for > 3 weeks prior to tumour resection and clinical samples pre/post-surgery are examined in the CCRC laboratory for the presence of the test bacteria. The outputs of this study stand to validate the clinical potential for bacterial-mediated treatment and/or diagnosis of cancer via ingestion of food-grade bacteria.

The authors wish to acknowledge support relevant to this manuscript from the Health Research Board and Breakthrough Cancer Research.

P: 81

The impact of CFTR modulation on CT Thoraces, circulating inflammatory mediators and sputum microbiome in a single centre cohort of patients with Cystic fibrosis with the G551D mutation

Submitting Author: Nicola Ronan

List of Authors: Ronan NJ (1,2), Einarsson G (3), O'Callaghan, G (1,2), Mooney D (3), , Elborn JS (3), NiChroinin M (1), Mullane D (1), Murphy DM (1,2), O'Connor OJ (4), Shortt C (1), Tunney M (3), Twomey M (4), Maher MM (4), Eustace JA (2), Plant BJ (1,2)

(1) Cork Cystic Fibrosis Centre, CUH/UCC
(2) HRB Clinical Research Facility, University College Cork
(3) CF & Airways Microbiology Research Group, Queen's University Belfast
(4) Department of Radiology, CUH/UCC

Discipline/Area: Cork Cystic Fibrosis Centre, CUH/UCC

Abstract:
Introduction: Ivacaftor produces significant benefit in patients with cystic fibrosis (CF) with the G551D mutation (1,2). Prevalence of this mutation at Cork University Hospital (CUH) is 23% (worldwide prevalence 4%) making it uniquely placed to provide single centre insight into CFTR modulation.

Methods: 33 Ivacaftor-naive Patients with CF (age ≥6) consented to routine quarterly clinical follow up (median 1 year follow up) where clinical changes pre and post-Ivacaftor were recorded. Three-monthly sputum, blood and low dose CT Thoraces were performed at baseline and post-Ivacaftor. Sputum bacteria were detected by plating on selective agars, quantified by total viable count and identified by PCR and sequencing of 16S rRNA genes. Circulating cytokines were measured in blood samples using an MSD platform. CT Thoraces were Bhalla scored.

Results: Significant mean improvements in FEV_1 (10.26%), BMI (1.2 Kg/m^2), Sweat test (-57.65 mmol/l), Respiratory Domain of CFQ-R (17.51 point), exacerbation rate requiring IV antibiotics were observed, with a significant increase in sputum diversity and richness (P <0.05) and ratio and a significant median reduction in circulating IL-6, IL-8, and IL-1β after 12 months of treatment. Improvement in CT Thoraces at 12 months were seen with a reduction in total Bhalla Score (P<0.005), airway wall thickening (P = 0.038), Consolidation (P=0.046) and extent of mucus plugging (P = 0.001).

Conclusion: In a large single centre cohort CFTR modulation is associated with a sustained improvement in clinical phenotype, decrease in inflammatory markers, change in lung microbiome and reduction in intraluminal bronchiectatic radiological complications.

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Funding: We would like to acknowledge funding from the European Commission for CFMATTERS, Grant agreement 603038

P: 82

Assessment of existing lay-person knowledge on the role and use of an Automated External Defibrillator in amateur sports clubs

Submitting Author: Paul Ryan

List of Authors: Ryan P, Falvey E.

Discipline/Area: Department of Medicine, University College Cork

Abstract:
Automated external defibrillators (AEDs) have become increasingly available in sports clubs, allowing members to defibrillate with minimal delay if necessary. However, it is unknown whether members of the public are sufficiently prepared or willing to use an AED. We therefore wished to investigate knowledge and attitudes among club members toward AEDs, and also examine the potential benefits of an interventional educational programme in increasing awareness and willingness to use an AED.

We visited a number of selected Cork GAA clubs and asked participants aged 16 and over to complete a 23-point questionnaire relating to current awareness and attitudes towards AEDs, and their willingness to use the device. Each participant then attended a 90-minute small-group teaching session where they were educated on the role and use of an AED, with opportunity to practice AED use in a controlled environment. After receiving teaching, each individual again completed the questionnaire.

The results of the study outline the baseline level of knowledge regarding AEDs among club members. Results will focus on the comparison of attitudes and knowledge levels in the same population before and after participation in the teaching course. This will allow evaluation of the potential role that an educational programme may have in improving first responder confidence and willingness to use an AED. The results will provide an insight into how structures relating to AED use in amateur sports clubs can be improved to optimise response to an emergency situation and maximise life-saving potential.

Funding Acknowledgement: UCC Summer Undergraduate Research Experience (SURE) Award.

P: 83

Inflammation and gut permeability: implications for health and disease

Submitting Author: Zeina Sabra

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(3) APC Microbiome Institute, University College Cork
(4) Department of Psychiatry, University College Cork

Discipline/Area:

Abstract:
Introduction: Irritable bowel syndrome (IBS) and Inflammatory bowel disease (IBD) are common functional gastrointestinal disorders (FGIDs)[1] ,IBS has a high prevalence in woman of reproductive age[2]. Patients typically report abdominal pain, bloating, constipation or diarrhea[3] . Many studies indicated an increase in the gut permabitly in IBS patients[4] .Intestinal permeability can be assessed using circulating markers such as intestinal fatty acid binding proteins. The consequences of increased intestinal permeability can be determine by assessing circulating anti-endotoxin antibodies, inflammatory markers (e.g. cytokines) and plasma tryptophan availability. ethical committee approval was permited to conduct testing .

Methods: This study was conducted on 29 healthy females (control),33 IBS patients, 16 IBD patients, matched on the basis of age. Proinflammatory Cytokine Sampling & Analysis: Plasma levels of IL-6, IL-8, and TNF-α were assayed in duplicate using a high sensitivity commercially available electrochemiluminescence MULTI-SPOT® Meso Scale Discovery kit (MSD, Rockville, MD, USA) as per the manufacturer's instructions. Kynurenine and Tryptophan Analysis*:* Plasma samples were spiked with internal standard (3-Nitro l-tyrosine) prior to being deproteinised by the addition of 20 µl of 4M perchloric acid to 200 µl of sample. Samples were centrifuged at 21000g on a Hettich Mikro 22R centrifuge (AGB, Dublin, Ireland) for 20 minutes at 4°C and 100 µl of supernatant transferred to a HPLC vial for analysis on the HPLC system (UV and FLD detection). Lipopolysaccharide-Binding protein(LBP): Plasma levels of LBP were assayed in duplicate using an immunoassay kit after removing the samples from -80 to room temperature.

Results: plasma IL-8 (p=0.038) and Kynurenine : Tryptophan ratio (p=0.001) and LBP (p=0.030) was significantly elevated in IBD patients vs. controls .Conclusion: GI disorders cause an increase in the gut permeability ,LBP can be used as a biomarker for identification of gut permeability in GI disorders such as IBD and this can be used as a safe test in vulnerable populations i.e. pregnant patients, next stage of the testing will be testing the effect of IBS on these biomarkers during pregnancy and the effects of the disorder on mother and infant health.
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P: 84

Development of Tumour Therapy and Imaging Strategies Utilising Bacteria

Submitting Author: Mike Stanton

List of Authors: Stanton M, Cronin M, Lehouritis P, Tangney M

Discipline/Area: Cork Cancer Research Centre, UCC, Cork

Abstract:
The ability of systemically administered bacteria to target and replicate to high numbers within solid tumours allows for the targeted activation of therapeutics and the confinement of therapeutic effect to the tumour site. For example, bacterial directed activation of a prodrug specifically within a tumour permits effective and specific localised tumour therapy. In order to monitor therapeutic activity, there is a requirement for the development of non-invasive imaging strategies to track bacteria within a live host. Optical imaging is the most commonly utilised preclinical imaging system. To date, the vast majority of non-invasive *in vivo* imaging systems for bacteria have relied on the use of bacteria that have been genetically modified or harbour genetic expression constructs. However, the use of engineered bacteria is often not experimentally appropriate or technologically feasible as engineering tools are not available for a number of bacterial strains. Therefore, there is a need for the development of optical imaging strategies using unmodified bacteria. Our work aims to develop novel therapeutic and non-invasive imaging strategies based on the endogenous enzymatic activity of tumour targeting bacteria. Nitroreductases are a family of bacteria-specific enzymes that are capable of activating the fluorescent probe CytoCy5S as well as the cytotoxic prodrug CB1954. *In vitro* and *in vivo* data demonstrate that endogenous levels of these enzymes are sufficient for probe activation and elicitation of a therapeutic effect in BALB/c mice bearing subcutaneous CT26 tumours. This study introduces the concept of utilising endogenous nitroreductases for therapeutic effect and as a reporter for wild-type bacteria. The system may be adapted for use with other imaging modalities or for other research fields such as infectious disease.

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P: 85

A combination of cytokines and LPS increase pro-inflammatory chemokine expression primary bronchial epithelia cells

Submitting Author: Ashley Sullivan

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**= Joint Supervisors*

Discipline/Area: Schools of Medicine and Microbiology, APC Microbiome Institute, University College Cork

Abstract:
In the asthmatic airway the epithelium lining the bronchi release many cytokines and chemokines resulting in the ensuing pathogenesis. While the role of inflammatory cytokines, such as IL-4 and IL-17, has been described in the asthmatic lung, little knowledge exists on the role microbial components play in asthmatic airway pathogenesis.

Our aim was to determine the effect cytokines and microbial components have on inflammatory gene expression on airway epithelium.

Primary bronchial epithelial cells (PBEC) were cultured from Bronchial brushing cultured from asthmatic patients and BEAS2B lung epithelial cells were stimulated with Th2 cytokines and microbial components and patient cell free bronchoalveolar lavage (BAL). RNA was extracted and qRT-PCR was used to determine the cytokine mRNA expression levels.

Our results to date suggest that the presence of cytokines in combination with microbial components induce lung epithelial inflammatory chemokine responses. IL-17 and IFNg in combination with LPS induce significant CCL2 and CCL20 expression (n=3). Patient BAL also induces elevated PBEC chemokine expression.

Our results demonstrate that the combination of immune stimuli in conjuction with microbial components is required to induce PBEC mediated inflammatory signalling. These observations may help in dissecting the pathogensis of asthmatic airway activation.

Funding for this project has been provided by the Wilton Research fund and a HRB summer studentship.

Ethical Permission has been granted for these studies.

P: 86

Membrane sweep at term gestation in CUMH; a case-control study

Submitting Author: Siun Sweeney-Landers

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Abstract:
Introduction: Sweeping the membranes is an obstetric procedure thought to reduce pregnancy duration, by hastening the onset of labour. However, the efficacy of the procedure has been disputed within the literature. Therefore, our study compared total pregnancy duration, interval to labour, and need for formal methods of induction, between study and control groups, in order to determine just how effective the procedure is.

Methods: This retrospective case control study examined 250 women, who attended Cork University Hospital from May to July 2015. The study group had been swept whilst the control group had not. SPSS and StatPlus were employed to analyse the data, using t-tests for continuous data and Chi square tests for categorical data.

Results: The mean gestation was greater in those who had their membranes swept, 284.02 days (CI 273.25 - 295.29) vs 281.55 days (CI 273.175 - 290.27) in those not swept, P value 0.003. The mean interval to labour was greater in the study group, 5.02 days (CI 4.25 - 6.29) vs the control group, 4.41 days (CI 4.18 - 4.99), P value 0.25. The procedure did not have a significant effect on the need for formal methods of induction with 33% of those swept being formally induced, whilst 37% of the control group were formally induced, P value 0.67.

Conclusion: Sweeping the membranes is ineffective at reducing overall pregnancy duration and interval to labour. There is a small reduction in the need for formal induction, in those swept, but it is not statistically significant.

P: 87

Examining the relationship between prenatal maternal stress and anxiety with gastrointestinal function in a population of nulliparous pregnant women

Submitting Author: Katie Togher

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Discipline/Area Department of Obstetrics and Gynaecology & Department of Psychiatry, University College Cork

Abstract:
Introduction: Gastrointestinal symptoms including nausea, vomiting and abdominal pain are commonly reported during pregnancy. Many studies have reported alterations in gastrointestinal function to be associated with high stress and anxiety. However this relationship has yet to be examined during pregnancy.

Methods: In this cohort study, 106 nulliparous pregnant women were recruited from the IMPROvED consortium at Cork University Maternity Hospital. The short version of the Speilberger State-Trait Anxiety Inventory (STAI) and the Perceived Stress Scale (PSS) were completed by participants between 19 – 22 weeks gestation. Gastrointestinal function was assessed using the Rome III module for diagnosing functional gastrointestinal disorders.

Results: The mean stress and anxiety score in this population were 11.8 and 4.73 respectively. Women were categorized as high and low stress if they scored greater than 18 or less than 7 on the PSS respectively. Participants were deemed to be highly anxious with a score greater than 8 or not anxious with a score less than 1 on the STAI. Women in the high stress or anxiety group were more likely to report abdominal pain and discomfort than their low stressed counterparts. Dissatisfaction with bowel habits and interference with lifestyle were more frequently reported among the high stress and anxiety groups.

Conclusion: This study suggests a correlation between prenatal stress and anxiety and gastrointestinal function. A better knowledge of the relationship between maternal stress and gastrointestinal function in pregnancy will help elucidate how maternal physiology is altered by prenatal stress and anxiety.

Ethical Approval: This study received ethical approval from the Clinical *Research Ethics* Committee of the *Cork Teaching Hospital.*

Funding: Alimentary Pharmabiotic Center (APC) and Irish Centre for Fetal and Neonatal Translational Research (INFANT)

P: 88

PHARMS Study (Patient Held Active Record of Medication Status)

Submitting Author: Elaine Walsh

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Discipline/Area: Department of General Practice, University College Cork

Abstract:
Introduction: Medication errors are a major source of preventable morbidity, mortality and cost (1, 2). The primary-secondary care interface at time of hospital discharge has been associated with medication error (3). Key areas within the error process have been identified as legibility, inadequate documentation and poor communication between healthcare professionals (4, 5, 6). To address these issues within a healthcare system which uses mixed paper/electronic records, a secure password protected electronic patient held medication record has been developed by a GP software provider (Si-Key Ltd) with collaboration from the departments of General Practice, Technology Transfer, INSIGHT and the Tyndall Institute.

Aims: To establish acceptability and usefulness of a patient held medication record from the perspectives of patients, hospital doctors and GPs and to ascertain if medication error can be reduced at time of hospital discharge.

Methods: A non-randomised feasibility study will be conducted among community dwelling patients of 3 urban GP practices taking 4 or more medications who are admitted to 2 medical wards of the Mercy University Hospital. The patient held medication records will be linked to the medication record in primary care and subsequently used by the hospital doctor to access the patient's pre admission medication list at time of generation of the discharge prescription. Semi-structured interviews will be conducted with patients, hospital doctors and GPs. Prevalence of prescribing errors will be estimated using RCGP guidelines and Controlled Drug legislation (6, 7).
Funding for the study has been granted by MediSec Ltd and the Strategic Research Fund, UCC.

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(1) Institute of Medicine report: "To Err is Human: Building a Safer Health System" IOM 1999
(2) Field TS, Gilman B et al. The costs associated with adverse drug events among older adults in the ambulatory setting. Med Care 2005; 43: 1171-6
(3) Grimes T et al. Survey of medication documentation at hospital discharge. Implications for patient safety and continuity of care. Ir J Med Sci 2008; 177: 93-97.
(4) Sander D. Borgsteede, Karapinar-Çarkit F et al. Information needs about medication according to patients discharged from a general hospital. Patient Education and Counseling. 2011; 83: (1)22–28.
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(6) Avery A J et al. Research into practice: safe prescribing. British Journal of General Practice 2014; 5: 259-261
(7) Misuse of Drugs Act 1971(2012)

P: 89

Economic impact of medication error: a systematic review

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Discipline/Area: Department of General Practice, University College Cork

Abstract:
Introduction: Medication error is a significant source of preventable morbidity and mortality among patients (1). Clinical and cost-effectiveness evidence are required for the implementation of interventions to improve quality of care in the health care sector. In the case of interventions to reduce medication error, reduction of cost due to error is a key potential benefit.

Aim: To quantify and describe the economic burden associated with errors during the medication use process.

Methods: A systematic review of the literature included the following databases: PubMed, Cochrane, Embase, CINAHL, EconLit, ABI/INFORM and Business Source Complete. Studies published between 2004 and 2015 defining medication error as “any preventable event that may cause or lead to inappropriate medication use or patient harm” (2) were included. Study quality was assessed using the Newcastle-Ottawa scale (3). A narrative synthesis was performed.

Results: 14 studies were deemed eligible for inclusion with 4 achieving a high score on the quality assessment scale. 13 studies expressed economic impact in monetary terms and cost per medication error ranged from €2.29 to €93, 415.24. 4 studies included costs incurred in primary care. All studies measured direct costs with 2 studies measuring additional indirect or opportunity costs.

Conclusion: Considerable variability existed between studies in terms of financial cost and many were of poor quality. Assessment of economic impact was conducted predominantly in the hospital setting with little assessment of impact in primary care. Limited parameters were used to establish economic impact and patient and societal economic impact was not explored.

References:
(1) Institute of Medicine report: "To Err is Human: Building a Safer Health System" IOM 1999
(2) Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation and reporting. Ann Intern Med. 2004; 140:795–801
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P: 90

Analysis of the molecular and cellular mechanisms regulated by magnesium sulphate in an in vitro model of the human placenta

Submitting Author: Rachel Williamson

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Discipline/Area: The Irish Centre for Fetal and Neonatal Translational Research (INFANT), CUMH

Abstract:
Introduction: Pre-eclampsia is a multi-systemic pregnancy disorder which globally affects 2-8% of all pregnancies. Magnesium sulphate ($MgSO_4$) is commonly administered for the prevention and treatment of life-threatening seizures in pre-eclamptic women and for fetal neuroprotection before anticipated preterm birth. We have developed an *in vitro* placental model to investigate the effects of $MgSO_4$ on mediating cytotrophoblast differentiation and placental inflammation.

Methods: Cytotrophoblast viability was examined post treatment with Lipopolysaccharide (LPS) and $MgSO_4$ by MTT assay. Pyknotic nuclei morphology was identified by immunofluorescence. Syncytial formation was assessed by desmoplakin architectural staining of cells treated with MgSO4 and LPS for 72hours. Real-time PCR was used to evaluated ACVR2A mRNA and TNF-α mRNA expression.

Results: $MgSO_4$ had a dose dependant effect on cytotrophoblast viability. Cytotrophoblasts treated with 200ng/ml LPS had significantly reduced cell viability (63%) after 48hrs. 1mM MgSO4 pre-treatment of cells rescued viability (79%) compared to controls. Similarly, 1mM $MgSO_4$ pre-treatment reduced development of pyknotic nuclei compared to controls. $MgSO_4$ reduced mRNA expression of ACVR2A and TNF-α. Finally $MgSO_4$ may alter cytotrophoblast differentiation.

Conclusion: $MgSO_4$ provides protection against LPS-induced inflammation by modulating syncytialisation and reducing pro-inflammatory cytokine expression *in vitro*.

Funding: Science Foundation Ireland

P: 91

Sugar On Trial: A Comparative Study to Assess the Relative Sweetness of Beet and Cane Sugar and the Resultant Potential for Sugar Reduction

Submitting Author: Eve Casey and Cathy Hynes. Kinsale Community Secondary School, Cork

Abstract:
Background: On the background of obesity and diabetes epidemics and their association with bad dietary habits, this project aims to reduce the amount of sugar that people use when making baked goods.

Methods: We used chemical tests, and consumer sensory tests to compare cakes made with beet and cane sugar for appearance, aroma, texture, sweetness, flavour, overall acceptability and consumer preference of the two cakes. Furthermore, we carried out blinded consumer testing of cakes containing varying amounts of sugar to assess consumers' preferences for varying degrees of sweetness.

Results: In blinded sensory consumer tests participants found cakes baked with cane sugar to be sweeter than cakes baked with beet sugar (95% confidence).
People's preference for cakes increased in line with increasing sugar content and this dose-response curve was strongly correlated with an R2 value of 0.97596.
We saw a definite trend of our youngest and oldest participants preferring the sweetest cake;
Despite people's preference for sweeter cake, there was a high acceptability rate for cakes made with reduced sugar content, which offers huge potential for sugar reduction and resultant health benefits.
In subsequent un-blinded testing we found that if participants were informed of the sugar content of the cakes, they were significantly more likely to prefer cakes with lower sugar content. This is a demonstration of a positive Halo Effect.
In summary, we know from our research that when people choose to consume a particular product for a period of time, for health or other benefits, that product becomes their new preferred norm. This phenomenon is known as the Mere Exposure Paradigm and could further potentially increase the acceptability of low sugar products.

Project won Science Foundation Ireland prize 2015 for the project "most likely to have an impact on Irish society" at BT Young Scientist and Technology Exhibition, Junior Biological and Ecological Section.

Notes: