7th December 2017

New Horizons in Medical Research
A Scientific Conference organised by the School of Medicine, Research and Postgraduate Affairs Committee, UCC.

Main Atrium, Western Gate Building, University College Cork
Dear Friends and Colleagues,

On behalf of the School of Medicine’s Research and Postgraduate Affairs Committee [RPAC] it is with great pleasure that I welcome you all to the New Horizons Medical Research Conference 2017. 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 of Medicine. 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 from within the School of Medicine. As a result, the event has been awarded six CPD points from the RCPI. We hope that all of today’s participants, students and staff enjoy the conference programme, as well as the hospitality of University College Cork during the event.

RPAC would like to extend its gratitude to our colleagues who presented* and chaired# the conference on sessions. RPAC would also like to express its gratitude to those who participated in judging the oral˟ and poster˟ presentations:

Dr Orla Barry˟  
Mr. Pat Casey*  
Dr Conan Connelly*  
Dr Eileen Duggan˟  
Dr Patricia FitzGerald˟  
Dr Zubair Kabir˟  
Dr Elizabeth Kenny-Walsh˟  
Ms Charlotte Merrett˟  
Dr Olivia O’Leary#  
Dr Colm O’Tuathaigh˟  
Dr Andre Toulouse˟️  
Dr Elizabeth Brint˟️  
Dr Gerard Clarke#  
Dr Suzanne Cremin*  
Dr Éanna Falvey*  
Dr Collette Hand*  
Professor Louise Kenny*  
Dr John MacSharry#  
Dr Yvonne Nolan*  
Dr Dervla O’Malley?  
Dr Derek Power*  
Dr Gabriella Rizzo#

Yours sincerely,

Liam J. Fanning, PhD, DSc  
Chair, School of Medicine Research & Postgraduate Affairs Committee, UCC  
https://www.ucc.ie/en/medical/research/committee/rpaccommiteemembers/
# New Horizons 2017

## Schedule at a Glance

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.00 a.m.</td>
<td>Free registration commences</td>
</tr>
<tr>
<td>8.00 a.m.</td>
<td>Hanging of posters in the main atrium WGB</td>
</tr>
<tr>
<td>8.55 a.m.</td>
<td><strong>Welcome Address:</strong> Dr Liam Fanning, Chair, School of Medicine Research &amp; Postgraduate Affairs Committee, UCC</td>
</tr>
</tbody>
</table>

## Session 1

**Chairs:** Dr Andre Toulouse and Dr Gabriella Rizzo

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.00 a.m.</td>
<td>Dr Yvonne Nolan, Department of Anatomy and Neuroscience, UCC</td>
<td>Lifestyle factors shaping hippocampal structure and function across the lifespan</td>
</tr>
<tr>
<td>9.25 a.m.</td>
<td>O1. Does Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Mellitus Predict Poor Long-Term Glycaemic Control. <em>Ms Louise Kelly, et al</em></td>
<td></td>
</tr>
<tr>
<td>9.55 a.m.</td>
<td>Dr Derek Power, Oncology Clinical Trials Unit, UCC</td>
<td>Cancer cachexia, sarcopenia, survival and quality of life in ambulatory oncology patients</td>
</tr>
<tr>
<td>10.20 a.m.</td>
<td></td>
<td>O4. Impact of Functional Vitamin D Deficiency on Perinatal Outcomes, <em>Ms Andrea Hemmingway, et al</em></td>
</tr>
<tr>
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<td></td>
<td>O6. Pre-operative visceral adiposity and pro-inflammatory adipokine levels influence early oncological outcomes in colon cancer, <em>Ms Christina Fleming, et al</em></td>
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<tr>
<td>10.50 a.m.</td>
<td></td>
<td>COFFEE and Viewing of Posters in Western Gateway Building Atrium</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
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<tr>
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<tr>
<td>11.15 a.m.</td>
<td><strong>Dr Cathal McCarthy</strong>, Department of Obstetrics and Gynaecology, UCC</td>
<td></td>
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<tr>
<td></td>
<td>Oxidative Stress and Pre-Eclampsia: Are we looking in the wrong place?</td>
<td></td>
</tr>
<tr>
<td>11.40 a.m.</td>
<td>O7. Respiratory control in the mdx mouse model of Duchenne muscular</td>
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<tr>
<td></td>
<td>dystrophy, <em>Mr David Burs, et al</em></td>
<td></td>
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<td></td>
<td>O8. Detecting the presence of Aspergillus in the asthmatic airway and</td>
<td></td>
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<tr>
<td></td>
<td>its relationship to disease severity, <em>Ms Ashley Sullivan, et al</em></td>
<td></td>
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<td></td>
<td>O9. Three-minute short elevator type pitches:</td>
<td></td>
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<tr>
<td></td>
<td>i. UCC iGEM 2017 – MOOnShine, <em>Ms Chloe Darragh-Hickey, et al</em></td>
<td></td>
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<tr>
<td></td>
<td>ii. Barriers and Facilitators to Appropriate Antipsychotic Prescribing</td>
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<td></td>
<td>in Nursing Home Residents with Dementia, <em>Mr Kieran A. Walsh, et al</em></td>
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<tr>
<td>12.10 p.m.</td>
<td><strong>Dr Collette Hand</strong>, Department of Pathology, UCC</td>
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<tr>
<td></td>
<td>A Genetic Perspective on Neuromuscular Disease in Ireland</td>
<td></td>
</tr>
<tr>
<td>12.35 p.m.</td>
<td>O10. How to Improve Waiting Times in General Practice - A Survey of GPs,</td>
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<tr>
<td></td>
<td><em>Ms Roseanne Tobin, et al.</em></td>
<td></td>
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<td></td>
<td>O11. Scenario modelling analysis to assess the potential to increase</td>
<td></td>
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<td>polyphenol intakes in Irish adults, teens and children through a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>polyphenol-enriched beverage. <em>Ms Clara Heneghan, et al</em></td>
<td></td>
</tr>
<tr>
<td>12.55</td>
<td><strong>Pat Casey</strong>, GMO Compliance Officer &amp; Biological Safety Advisor, UCC</td>
<td></td>
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<tr>
<td></td>
<td>Biological Safety in UCC Research</td>
<td></td>
</tr>
<tr>
<td>1.05 p.m.</td>
<td>LUNCH and viewing of posters. Poster judging.</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>Session 3</td>
<td>Presenters/Details</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>2.00 p.m.</td>
<td>Dr Suzanne Cremin, STI Clinic, SIVUH</td>
<td>Trends and outbreaks of sexually transmitted infections in recent years.</td>
</tr>
<tr>
<td>2.30 p.m.</td>
<td>O12. An Augmented Prescribed Exercise Programme (APEP) for frail older medical inpatients in the acute setting: a randomised controlled trial. Ms Ruth McCaulagh, et al</td>
<td></td>
</tr>
<tr>
<td>2.30 p.m.</td>
<td>O13. Three-minute short elevator type pitches:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>i. Living Microbes Within Tumours. Mr Glen Hogan, et al</td>
<td></td>
</tr>
<tr>
<td>2.50 p.m.</td>
<td>Mr Cian Duggan, ATLANTIC CORRIDER WINNER, UCC</td>
<td>An exploration of the effectiveness of an educational intervention on the use of personal protective equipment in orthopaedic theatres</td>
</tr>
<tr>
<td>3.00 p.m.</td>
<td>Dr Éanna Falvey, School of Medicine, UCC</td>
<td>Research-Led Sports &amp; Exercise Medicine</td>
</tr>
<tr>
<td>3.30 p.m.</td>
<td>Dr Conan Donnelly, Research Manager, National Cancer Registry</td>
<td>The National Cancer Registry Ireland – A resource for real world research.</td>
</tr>
<tr>
<td>3.50 p.m.</td>
<td>Prize giving and meeting close</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Professor Denis O’Mahony,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>School of Medicine, UCC</td>
<td></td>
</tr>
<tr>
<td>Page</td>
<td>Content</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Summary of Oral Presentation Abstracts</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Oral Presentation Abstract details</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Summary of Poster Presentation Abstracts</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Poster Presentation Abstract details</td>
<td></td>
</tr>
<tr>
<td>114</td>
<td>Notes</td>
<td></td>
</tr>
</tbody>
</table>
### Oral Presentations: G05 Western Gateway Building UCC

O = Oral Number

<table>
<thead>
<tr>
<th>O</th>
<th>Author</th>
<th>Abstract Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ms Louise Kelly</td>
<td>Does Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Mellitus Predict Poor Long-Term Glycaemic Control.</td>
</tr>
<tr>
<td>2</td>
<td>Ms Sarah Riis</td>
<td>Insulin-like Growth Factor-1 Signalling is essential for Mitochondrial Biogenesis and Mitophagy in Cancer Cells</td>
</tr>
<tr>
<td>3</td>
<td>Ms Grace O Regan</td>
<td>Is there an association between methods of self-harm and risk of self-harm repetition? Findings from the National Self-Harm Registry Ireland</td>
</tr>
<tr>
<td>4</td>
<td>Ms Andrea Hemmingway</td>
<td>Impact of Functional Vitamin D Deficiency on Perinatal Outcomes</td>
</tr>
<tr>
<td>5</td>
<td>Ms Elaine Enright</td>
<td>The impact of gut microbiota-mediated bile acid metabolism on drug uptake and activity in vitro</td>
</tr>
<tr>
<td>6</td>
<td>Ms Christina Fleming</td>
<td>Pre-operative visceral adiposity and pro-inflammatory adipokine levels influence early oncological outcomes in colon cancer</td>
</tr>
<tr>
<td>7</td>
<td>Mr David Burs</td>
<td>Respiratory control in the mdx mouse model of Duchenne muscular dystrophy</td>
</tr>
<tr>
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<td>Ms Ashley Sullivan</td>
<td>Detecting the presence of Aspergillus in the asthmatic airway and its relationship to disease severity</td>
</tr>
<tr>
<td>9 (i)</td>
<td>Ms Chloe Darragh-Hickey</td>
<td>UCC iGEM 2017 – MOOnShine</td>
</tr>
<tr>
<td>9 (ii)</td>
<td>Mr Kieran A. Walsh</td>
<td>Barriers and Facilitators to Appropriate Antipsychotic Prescribing in Nursing Home Residents with Dementia</td>
</tr>
<tr>
<td>10</td>
<td>Ms Roseanne Tobin</td>
<td>How to Improve Waiting Times in General Practice - A Survey of GPs</td>
</tr>
<tr>
<td>11</td>
<td>Ms Clara Heneghan</td>
<td>Scenario modelling analysis to assess the potential to increase polyphenol intakes in Irish adults, teens and children through a polyphenol-enriched beverage</td>
</tr>
<tr>
<td>12</td>
<td>Ms Ruth McCaullagh</td>
<td>An Augmented Prescribed Exercise Programme (APEP) for frail older medical inpatients in the acute setting: a randomised controlled trial</td>
</tr>
<tr>
<td>13 (i)</td>
<td>Mr Glen Hogan</td>
<td>Living Microbes Within Tumours</td>
</tr>
<tr>
<td>13 (ii)</td>
<td>Ms Rachel Furlong</td>
<td>Mechanisms by which PINK1 regulates cell survival signalling - exposing novel targets for the treatment of Parkinson’s disease</td>
</tr>
</tbody>
</table>
Does Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes Mellitus Predict Poor Long-Term Glycaemic Control

A Tuthill, LC Kelly

Department of Endocrinology, Cork University Hospital, Cork, Ireland

Introduction

Diabetic ketoacidosis (DKA) is an acute complication of type 1 diabetes.

Aims and Objectives

This study aimed to determine 1) whether DKA at diagnosis of type 1 diabetes is associated with poor long-term glycaemic control; 2) to establish whether there are confounding factors which may impact the mode of presentation or subsequent glycaemic control.

Methods

This study was conducted via review of 102 patient files extracted from the Young Person’s Diabetes Clinic at Cork University Hospital. DKA was defined as a venous pH<7.3 or a bicarbonate level<15 mmol/L. Glycaemic control was measured using the average of the patient’s three most recent HbA1C levels, a median of 11.5yrs post diagnosis.

Results

Preliminary analysis revealed a significant association between DKA at diagnosis and absent honeymoon phase, p = .044. No significant difference in glycaemic control at follow-up was found between individuals with DKA at diagnosis and no DKA, p > 0.05. Certain sociodemographic factors were found to predict worse glycaemic control at follow-up: Individuals using recreational drugs, those in contact with a social worker, and those reporting mental illness were found to have higher levels of HbA1C at follow up (p=0.013, p=.025, and p<0.05 respectively) compared to individuals who did not.

Discussion/Conclusion

Diabetic ketoacidosis at diagnosis of type 1 diabetes was shown to be associated with absent honeymoon phase in this study. Furthermore, individuals who utilise recreational drugs, have contact with a social worker or have a mental illness had significantly worse glycaemic control at follow-up.
Insulin-like Growth Factor-1 Signalling is essential for Mitochondrial Biogenesis and Mitophagy in Cancer Cells

S Riis¹, A Lyons¹, M Coleman¹, C Favre¹, C O'Flanagan³, A Zhdanov¹, D Papkovsky¹, S Hursting³, R O'Connor¹

¹School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland
²Division of Nutritional Biochemistry, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina, USA

Mitochondrial activity and metabolic reprogramming influence the phenotype of cancer cells and resistance to targeted therapy. Previously, we have shown that the IGF-1-inducible mitochondrial nucleotide carrier PNC1/SLC25A33 is essential for mitochondrial function, indicating a role for IGF-1 signalling in the regulation of mitochondrial homeostasis. This prompted us to investigate, whether IGF-1 signalling is essential for mitochondrial maintenance in cancer cells, and whether this contributes to therapy resistance.

We found that IGF-1 stimulated mitochondrial biogenesis through induction of the transcriptional co-activators PGC-1β and PRC in a range of cell lines. Suppression of PGC-1β and PRC with siRNA disrupted mitochondrial morphology and membrane potential. Of note, MCF-7 cells with acquired resistance to an IGF-1R tyrosine kinase inhibitor (MCF-7-R) exhibited reduced expression of PGC-1β and PRC and impaired mitochondrial biogenesis. Interestingly, the cells exhibited mitochondrial dysfunction indicated by reactive oxygen species (ROS) expression, reduced expression of mitophagy mediators BNIP3 and BNIP3L, and attenuated mitophagy.

In agreement with this, we demonstrated that IGF-1 stimulation induced the expression and mitochondrial accumulation of BNIP3. Additionally, IGF-1 induced expression of the Nrf2/NFE2L2 gene, which has been implicated in both mitochondrial biogenesis and anti-oxidant responses. Suppression of Nrf2 caused reduced induction of BNIP3 in response to IGF-1, suggesting a role for Nrf2 in IGF-1-mediated regulation of mitophagy.

We conclude that IGF-1 signalling is essential for sustaining cancer cell viability by stimulating both mitochondrial biogenesis and turnover. This core mitochondria protective signal is likely to strongly influence responses to therapy and the phenotypic evolution of cancer.
Is there an association between methods of self-harm and risk of self-harm repetition? Findings from the National Self-Harm Registry Ireland

G O'Regan<sup>1,2</sup>, P Corcoran<sup>1,2</sup>, D Leahy<sup>1,2</sup>, E Griffin<sup>1</sup>, C Dillon<sup>1</sup>, E Arensman<sup>1,2</sup>

<sup>1</sup>National Suicide Research Foundation, University College Cork, Cork, Ireland  
<sup>2</sup>Department of Epidemiology and Public Health, University College Cork, Cork, Ireland

**Background:** Intentional drug overdose is involved in two thirds of self-harm presentations to hospital and a further 25% of presentations are due to self-cutting. Engaging in self-cutting is associated with increased risk of self-harm repetition. This study examines the association between how people harm themselves and subsequent self-harm repetition.

**Methods:** Data on consecutive self-harm presentations to hospital (2010-2015) were obtained from the National Self-Harm Registry Ireland. Associations between method characteristics and self-harm repetition were analysed using survival analysis.

**Results:** During the study period, 55,756 self-harm presentations were recorded involving 40,639 individuals. The majority of self-harm presentations involved intentional drug overdose (68.6%) followed by self-cutting (23.3%). In univariate analyses, overdoses involving more than 30 tablets and poly-drug overdoses were associated with increased risk of subsequent repetition compared to overdoses involving less than 30 tablets and one drug only. Overall, self-cutting was associated with increased risk of repetition. Severe self-cutting involving sutures or surgical referral was associated with reduced risk of repetition compared to less severe or superficial self-cutting. Compared to all other methods, lower risk of repetition was found following self-poisoning with chemical substances, self-harm using a firearm, and intentional crashing of a motor vehicle, methods associated with high lethality. In contrast, self-harm involving a blunt object was associated with increased risk of repetition.

**Discussion:** Detailed consideration of method of self-harm should form part of psychosocial and psychiatric assessments and planning of follow-up care for self-harm patients. Recommended treatment should be tailored according to patient needs and risk of subsequent suicidal behaviour.
Impact of Functional Vitamin D Deficiency on Perinatal Outcomes

A Hemmingway\textsuperscript{1,2}, LC Kenny\textsuperscript{2,3}, ME Kiely\textsuperscript{1,2}

\textsuperscript{1}Cork Centre for Vitamin D and Nutrition Research, University College Cork, Cork, Ireland
\textsuperscript{2}The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork, Ireland
\textsuperscript{3}Department of Obstetrics and Gynaecology, University College Cork, Cork, Ireland

Vitamin D deficiency, prevalent worldwide in pregnancy, has been associated with adverse perinatal outcomes. Although vitamin D is integral to the calcium metabolic system, the two nutrients are often examined independently. Functional vitamin D deficiency [deficiency plus elevated parathyroid hormone (PTH)], indicative of calcium metabolic stress, may impact on perinatal health. We aimed to test this through exploration of associations of vitamin D and PTH with clinically validated outcomes [mean arterial pressure (MAP), preeclampsia (PE) and small-for-gestational-age (SGA)].

Serum 25-hydroxyvitamin D [25(OH)D], the vitamin D status biomarker, was measured at 15 weeks’ gestation by LC-MS/MS and iPTH by ELISA in 1,714 well characterised, white, nulliparous, low risk SCOPE Ireland participants. Elevated MAP was defined as >90mmHg. Following exclusion of those >97.5\textsuperscript{th} percentile (to minimise inclusion of undiagnosed primary hyperparathyroidism cases), elevated PTH was defined as >80\textsuperscript{th} percentile. We classified functional vitamin D deficiency as 25(OH)D <30nmol/L+PTH 80-97.5\textsuperscript{th} percentile (n=94) and vitamin D repletion as 25(OH)D ≥75nmol/L+PTH ≤80\textsuperscript{th} percentile (n=373).

The prevalence of elevated MAP was 9.7\% among replete women and 19.1\% in women with functional vitamin D deficiency [AOR 2.30 (1.08, 4.90)]. In replete participants 1.9\% and 6.7\% had PE or a SGA birth respectively, compared with 4.3\% and 16.0\% of those with functional vitamin D deficiency. AORs were 1.10 (0.29, 4.17) for PE and 1.59 (0.75, 3.35) for SGA. To conclude, these results highlight the importance of considering vitamin D within the broader calcium metabolic system in future explorations of nutrition and perinatal outcomes.
The impact of gut microbiota-mediated bile acid metabolism on drug uptake and activity in vitro

EF Enright\textsuperscript{1,2}, K Govindarajan\textsuperscript{2}, R Darrer\textsuperscript{2}, BT Griffin\textsuperscript{1}, SA Joyce\textsuperscript{2,3}, CGM Gahan\textsuperscript{1,2,4}

\textsuperscript{1} School of Pharmacy, University College Cork, Cork, Ireland  
\textsuperscript{2} APC Microbiome Institute, University College Cork, Cork, Ireland  
\textsuperscript{3} School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland  
\textsuperscript{4} School of Microbiology, University College Cork, Cork, Ireland

Once regarded obscure and underappreciated, the cohabitation of man and microbe has gained increasing recognition as a determinant of host health. Pharmacokinetic research at the host-microbe interface has been primarily directed towards effects on metabolism. Bile acids (BAs) are synthesized by the host and biotransformed (deconjugated and dehydroxylated) by gut bacteria. The objective was to elucidate possible mechanisms by which BAs, traditionally regarded to be surfactants, could affect intestinal drug uptake. Now recognized as signalling molecules, this study investigated if host and microbial BAs could differentially influence the expression of intestinal drug transporters and thereby drug uptake.

The impact of microbial BA metabolism on influx and efflux transporter (including ABCB1, encoding P-gp) expression in Caco-2 cells was assessed. The ability of host (conjugated) and microbial (deconjugated/dehydroxylated) BAs to differentially affect drug uptake/activity was investigated using the P-gp substrates, cyclosporine A (CsA) and rhodamine 6G. Cell viability was used as a preliminary marker of altered CsA uptake/activity. Potential mechanisms by which BAs could affect P-gp functioning was evaluated using ATPase and bidirectional transport assays.

Unconjugated BAs significantly augmented CsA toxicity and reduced rhodamine 6G efflux, compared to tauro-conjugates. These effects could not be explained by changes to ABCB1 mRNA transcripts. BAs were determined to inhibit, rather than stimulate, basal P-gp ATPase suggesting a non-competitive interaction with the transporter.

Microbial BA metabolism was demonstrated to affect the uptake/activity of efflux substrates. The physicochemical properties of unconjugated bile acids, including their capacity for passive membrane diffusion, is speculated to underpin their preferential attenuation of P-gp efflux.
Pre-operative visceral adiposity and pro-inflammatory adipokine levels influence early oncological outcomes in colon cancer

CA Fleming\textsuperscript{1,2}, EP O'Connell\textsuperscript{1,2}, DP O'Leary\textsuperscript{1,2}, JH Wang\textsuperscript{1,2}, HP Redmond\textsuperscript{1,2}

\textsuperscript{1}Surguvant Research Centre, Cork University Hospital, Cork, Ireland. 
\textsuperscript{2}Department of Academic Surgery, Cork University Hospital, Cork, Ireland.

\textbf{Introduction:} Obesity and inflammation are independently associated with poor prognosis in colorectal cancer. It may be postulated that obesity can further potentiate the effect of inflammation on cancer outcomes. We aimed to identify if pre-operative visceral adiposity and pro-inflammatory adipokines influence outcomes in colon cancer.

\textbf{Methods:} Patients with non-metastatic colon cancer presenting for elective resection were prospectively enrolled. Exclusion criteria included: active/chronic infection; chronic inflammatory conditions; anti-inflammatory/steroid use. Pre-operative cytokine levels were measured using ELISA technique. Volumetric measurement of total (TF), visceral (VAT) and subcutaneous (SAT) adiposity at lumbar level using standard CT technique and OsiriX software was performed. Ratio of visceral to total fat area (VAT:TF) was calculated as a marker of adiposity. Statistical analysis was performed using SPSS, v.22.

\textbf{Results:} Twenty-six patients were included. Mean age was 67 years (range 29-85 years). Included AJCC colon cancer stages were: III [53.8\%, (n=15)]; II [38.5\%, (n=10)]; I [7.7\%, (n=2)]. High VAT:TF was significantly associated with post-operative complications (p=0.04), in particular post-operative infection (p=0.03), independent of gender, operative approach, perioperative antibiotic used and standard pre-operative BMI. High VAT:TF (p=0.036) and high pre-operative IL-6 (p=0.003) were both significantly associated with early colon cancer recurrence (<2 years). High VAT:TF (p=0.002) and high pre-operative IL-2 levels (p=0.043) were also associated with cancer-related mortality within 2 years.

\textbf{Conclusion:} High visceral adiposity and adipokine levels influence early patient oncological outcomes in colon cancer.
Respiratory control in the mdx mouse model of Duchenne muscular dystrophy

DP Burns¹, A Roy², EF Lucking¹, FB McDonald², RJ Wilson², DD Fuller³, D Edge⁴, KD O’Halloran¹

¹Physiology, University College Cork, Cork, Ireland
²Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada
³Centre for Respiratory Research and Rehabilitation, University of Florida, Gainesville, FL, USA
⁴Physiology, Trinity College Dublin, Dublin, Ireland

Duchenne muscular dystrophy (DMD) is a fatal neuromuscular disease. DMD morbidity relates to profound skeletal muscle weakness that extends to the respiratory muscles. DMD culminates in respiratory failure, yet there is a paucity of information regarding respiratory control in pre-clinical models of DMD. We sought to perform a comprehensive analysis of the respiratory control system in a murine model of DMD---the mdx mouse.

Young male wild-type and mdx mice were studied to examine ventilation by plethysmography. Carotid body afferent discharge was determined in perfused ex vivo preparations. Diaphragm EMG activity was recorded under basal conditions and in response to chemostimulation under anesthesia. Diaphragm ex vivo force-generating capacity, and muscle fibre size and distribution were determined.

During normoxia, mdx mice hypoventilated (decreased \( V_E/VCO_2 \)), owing to a reduction in tidal volume, with no change in metabolism. Carotid body discharge was lower in mdx mice, but chemoafferent responses and ventilatory and metabolic responses to hypoxia were equivalent. Diaphragm force was severely depressed in mdx mice, with evidence of central nucleation, fibre remodeling and damage, and increased fibrosis. Diaphragm EMG responses to asphyxia were enhanced in mdx mice suggesting compensatory neuroplasticity facilitating ventilation during chemostimulation. We have established interventional drug treatments which completely restore ventilation and diaphragm function in mdx mice.

We reveal that respiratory control is altered in the young mdx mouse model, with relevance to human DMD. Interventional studies employing antioxidant and anti-inflammatory/anti-stress strategies are yielding promising data.
Detecting the presence of Aspergillus in the asthmatic airway and its relationship to disease severity

A Sullivan1,3, EB Hunt2,5, S Lapthorne1, C Ward4, J Eustace5, PM O'Byrne6, BJ Plant2,5, DM Murphy2,5*, J MacSharry1,3*

1APC Microbiome Institute, UCC, Cork, Ireland
2The Department of Respiratory Medicine, Cork University Hospital, Cork, Ireland
3Schools of Medicine and Microbiology, UCC, Cork, Ireland
4Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK
5HRB funded CRFC, UCC, Cork, Ireland
6The Michael G DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada

Respiratory research is beginning to investigate the effects of host-microorganism interactions in the airway. Our aim was to determine if Aspergillus was detectable in the lower airways in a cohort of well-defined asthmatics and if so whether there was a relationship between its presence and asthma severity and level of disease control.

80 patients, stratified by asthma severity (GINA) and level of control (ACQ-7) were prospectively recruited. Blood serum was assessed for Aspergillus precipitins, Aspergillus RAST and IgE level and patients underwent bronchoscopy with bronchoalveolar lavage (BAL). Microscopy, cell differentials, DNA extraction and qPCR were performed on BAL to determine presence of Aspergillus.

Microscopic evaluation demonstrated the presence of Aspergillus in BAL. qPCR detected fungal presence in 84% of patient BAL and Aspergillus in >46% of patients. Asthma control (ACQ-7) was not associated with BAL aspergillus levels. Aspergillus levels in BAL correlated with BAL macrophage counts (%) (P<0.05). Aspergillus precipitins was associated with raised total fungal levels (p<0.05) but not Aspergillus levels in BAL.

Despite the presence of Aspergillus in almost half of our cohort (46%) we were unable to find any association between its presence and measures of asthma severity or control. Further studies are now required to assess whether or not aspergillus presence within the asthmatic airway has a pathological role in the disease.
Synthetic biology allows for the creation of biological sensors from pre-existing natural genetic circuits. Our project aims to create a standardised universal biosensor strategy, that will be affordable and user friendly, containing all the components for readout. This system will consist of three elements: a bioengineered construct, the chassis and the readout device.

1. Bioengineered Construct
Comprises a biological circuit designed to detect the presence of a specific substrate. This sensing element of each construct is specific to the substance being detected, while the readout from each construct is consistent = AmiCP (a blue coloured chromoprotein).

2. Chassis
The system is deployed initially through plasmid containing E. coli (tube-based), with the aim of progressing to a cell free system (as a lyophilised paper system).

3. Readout Device
The readout device has been 3D printed and is designed to attach to common smartphones. The device acts as a spectrophotometer, enabling easy measurement of the relative fluorescence or absorbance of a sample. Using a mobile app and algorithms developed by the team, the device compares the fluorescence/absorbance measurement to a standard curve and determines the concentration of the substance being tested for in the sample.

To validate the idea for our Universal Biosensor Strategy, we identified Irish industries with a need for such a product. We have targeted the dairy and microbrewery industries as proof of concept for our project, to test for antibiotic or methanol residue.
Barriers and Facilitators to Appropriate Antipsychotic Prescribing in Nursing Home Residents with Dementia

KA Walsh1,2,3, A Fleming1, C Sinnott4, J McSharry5, S Byrne1, J Browne2, S Timmons3

1Pharmaceutical Care Research Group, School of Pharmacy, University College Cork, Cork, Ireland
2School of Epidemiology and Public Health, University College Cork, Cork, Ireland
3Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork, Cork, Ireland
4Department of Primary Care and Public Health, University of Cambridge, Cambridge, United Kingdom
5School of Psychology, National University of Ireland, Galway, Galway, Ireland

Background: Antipsychotics are often inappropriately prescribed to nursing home residents with dementia despite evidence of increased risks and limited effectiveness, but can be effective when used for correct indications. This study aimed to explore the influences on appropriate antipsychotic prescribing in residents with dementia using the Theoretical Domains Framework (TDF), a theory-based approach to understanding key aspects of healthcare professionals’ behaviours.

Methods: Twenty-seven semi-structured qualitative interviews were conducted with a purposive sample of participants involved in the care of residents with dementia (four consultants, five general practitioners, eight nurses, two pharmacists, five healthcare assistants and three family members). An interview topic guide was developed using findings from our previous systematic review. Interviews were audio-recorded and transcribed verbatim. A qualitative framework analysis informed by the TDF, involving two coders, was conducted to identify the relevant barriers and facilitators.

Results: Nine TDF domains out of 14, were identified as relevant to antipsychotic prescribing behaviour. Barriers to appropriate prescribing included inadequate resources and education, pressure to prescribe, an expectation that behaviours can be “cured”, reliance on antipsychotics to reduce nursing demands, and the belief that residents are suffering because of their behaviours. Facilitators included specialist care units, advocacy and leadership by staff, knowledge of cardiovascular risks, and inclusive decision-making.

Conclusions: This detailed qualitative analysis demonstrates that appropriate antipsychotic prescribing is a complex behaviour influenced by several domains. Our study has generated much needed evidence to inform improvement efforts in this field.
How to Improve Waiting Times in General Practice - A Survey of GPs

TF Foley, RT Tobin

Department of General Practice, University College Cork, Cork, Ireland

Introduction Avoidance of prolonged waiting time is a priority for patients attending their general practitioner (GP). Prolonged pre-consultation waiting time is known to reduce consumer satisfaction, and hamper positive health-related outcomes. While the consequences of prolonged waiting time have been extensively investigated for patients, there is a paucity of published literature from the perspective of GPs.

Aims/Objectives The main aim of this study was to explore GPs opinions on prolonged waiting times in general practice. The key objectives were to identify GPs’ views on;

• The impact of prolonged waiting time on GPs
• Contributors to prolonged waiting time
• Solutions to prolonged waiting time

Methods A questionnaire was designed, piloted, revised and posted to 300 GPs who were randomly selected from the Irish Medical Directory. Questionnaires included four parts; Participant Demographics, Appointment Mechanisms, Contributors to prolonged waiting time, Solutions to prolonged waiting time. Ethical Approval was granted by Cork Research Ethics Committee.

Results 169/300 questionnaires were returned, giving a response rate of 56%. GPs acknowledged the challenges associated with extended waiting times and reported increased stress and tendency to rush during a consultation for which the patient had waited a prolonged period. Long consultations and chronic disease management were identified as major contributors to time delay. Three main strategies were identified to reduce waiting time: time for administrative tasks; catch-up slots, and nurse-led clinics.

Conclusion These findings suggest that prolonged waiting time is a significant area of concern for GPs. Policy and practice change is necessary in order to minimise negative impacts and improve working conditions. Future research should consider qualitatively exploring this sensitive issue and should also triangulate findings with the relevant voice of patients.
Scenario modelling analysis to assess the potential to increase polyphenol intakes in Irish adults, teens and children through a polyphenol-enriched beverage.

C Heneghan\textsuperscript{1}, A Hennessy\textsuperscript{1}, J Lyons\textsuperscript{1}, T Singh\textsuperscript{1}, J Walton\textsuperscript{2}, A Flynn\textsuperscript{2}, M Kiely\textsuperscript{1}, A Lucey\textsuperscript{1}

\textsuperscript{1}Cork Centre for Nutrition and Vitamin D Research, University College Cork, Cork, Republic of Ireland
\textsuperscript{2}School of Food and Nutritional Sciences, University College Cork, Cork, Republic of Ireland

The consumption of polyphenols may reduce the risk of major cardiovascular events by up to 46%. We have previously reported that beverages were the main source of polyphenols in the diets of Irish adults and teens. A novel polyphenol-enriched blackberry beverage (~280mg as gallic acid equivalents/100ml; 28kcal/100ml) was developed at University College Cork as part of the Cardio-Rubus project. A scenario modelling exercise was conducted to explore how polyphenol intakes in Ireland could be modulated if this novel “Rubus” blackberry polyphenol rich beverage was to be made commercially available.

We aimed to evaluate the effects of substituting commonly consumed polyphenol-containing beverages including tea, coffee, orange juice, apple juice and squash drinks with the “Rubus” beverage using a scenario modelling software available at Crème Nutrition\textsuperscript{©} and nationally representative food consumption data of Irish adults, teens and children (www.iuna.net).

When the “Rubus” beverage was substituted for tea at 10% and 20% of tea-drinking occasions, the mean (SD) intake of total polyphenols in Irish adults increased from 1008 (612)mg/d to 1242 (705)mg/d (+23%) and 1508 (1064)mg/d (+50%), respectively and in teens from 568 (419)mg/d to 632 (487)mg/d (+11%) and 699 (563)mg/d (+23%), respectively. The substitution of orange juice with the Rubus beverage in children produced increased intakes from 438 (238)mg/d to 470 (262)mg/d (+8%) and 503 (291)mg/d (+17%) at 10 and 20% of eating occasions, respectively. This study demonstrated that consumption of polyphenol-enriched functional beverages may represent an effective strategy to increase polyphenol intakes across multiple population groups.
An Augmented Prescribed Exercise Programme (APEP) for frail older medical inpatients in the acute setting: a randomised controlled trial.

R McCullagh1, E O’Connell2, S O’Meara3, K O’Connor4, D Dahly3, NF Hosgan5, S Timmons1

1Centre for Gerontology & Rehabilitation, School of Medicine, UCC@St Finbarr's Hospital, Cork, Ireland
2Physiotherapy Department, Mercy University Hospital, Grenville Place, Cork, Ireland
3Clinical Research Facility, School of Medicine, UCC@Mercy University Hospital, Grenville Place, Cork, Ireland
4Department of Geriatric Medicine, Mercy University Hospital, Grenville Place, Cork, Ireland
5School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland

Aim: To measure the effects of an augmented prescribed exercise programme on physical performance, quality of life and healthcare utilisation for frail older medical patients in the acute setting.

Methods: Within two days of admission, older medical inpatients with an anticipated length of stay ≥3 days, needing assistance/aid to walk, were blindly randomly allocated to the intervention or control group. Until discharge, both groups received twice daily, Monday-to-Friday, half-hour assisted exercises. The intervention group completed tailored strengthening and balance exercises; the control group, stretching and relaxation exercises. Length of stay and readmissions were recorded and physical performance (Short Physical Performance Battery), and quality of life (EuroQOL-5D-5L) were measured at discharge and at three months. Differences in length of stay (time-to-event) physical performance and quality of life (linear regression) were analysed.

Results: Data existed for 198 patients (aged 80 ±7.5). Groups were comparable at baseline. The difference in length of stay was not statistically different (HR 1.09 (CI, 0.77-1.56) p=0.6). With adjustment and exclusion of patients transferred to rehabilitation, the difference became clearer, but remained insignificant (n=125, HR 1.3 (CI, 0.9-1.87) p=0.16). Physical performance was better in the intervention group at discharge (adjusted, n=174, β=0.78 CI, 0.28-1.29) p=0.003). Small improvements in quality of life were detected in the intervention group at follow-up (adjusted, n=143, β=0.26 CI, 0.07-0.45) p=0.008.

Conclusion: The significant improvements in physical performance and quality of life suggest that this intervention is of value to frail medical inpatients. Its effect on length of stay remains unclear.
The recent discovery by our group of a bacterial presence within healthy and malignant human breast tissue has pointed towards the existence of a tumour microbiome. This microbiome has been described via deep sequencing techniques. However, while high-throughput sequencing can help to define the composition of a bacterial community, it is disadvantageous in that it cannot confirm the viability of the microbes it detects. Further work is therefore required to create a more comprehensive portrait of the breast microbiome, and to potentially obtain tumour-adapted bacteria from human tumours to serve as drug delivery vehicles.

Our aim in this study was to develop a culture-dependent system, capable of capturing as wide an array of bacteria as possible from murine and human tissues. A procedure was developed and optimised using murine tumour models, before applying to fresh patient samples. Multiple bacterial genera and species were cultured from patient breast tissue, unlike control samples for skin or environmental ‘background’. There was significant divergence in the profiles of murine and human tissues in terms of their bacterial make-up. To our knowledge, this is the first study in which viable bacteria have been recovered from human tumour tissue.
Mechanisms by which PINK1 regulates cell survival signalling – exposing novel targets for the treatment of Parkinson’s disease.

Ms RM Furlong\textsuperscript{1,2}, Dr A Lindsay\textsuperscript{1}, Prof AM Sullivan\textsuperscript{2}, Dr C O'Neill\textsuperscript{1}

\textsuperscript{1}School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland
\textsuperscript{2}Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

Parkinson’s disease (PD) is characterised by neuronal loss in the substantia nigra and striatum. Defects in cell survival and cellular health, in which the PI3-kinase/Akt pathway plays a major role, are strongly implicated in PD, and previous research in our lab showed that Akt activation is reduced in the PD brain. Moreover PD-causing genes, including loss of function of \textit{PINK1} (PTEN-induced putative kinase-1), may cause PD by impairing PI3-kinase/Akt signalling. Therefore, PINK1-modified cells are an extremely useful model to improve mechanistic understanding of how the PI3-kinase/Akt system becomes impaired in PD and to identify novel targets for therapeutic intervention. We show that Akt activity is significantly decreased in PINK1\textsuperscript{-/-} mouse embryonic fibroblasts. Our results further pinpoint loss of PINK1’s ability to activate Akt to be upstream of Akt activation via its phosphorylation, as neither PDK-1 and RICTOR (the major Akt activating kinases), nor PTEN, the major negative regulator of Akt, are affected by PINK1 expression. Further results show, for the first time, that reduced Akt activation in this PD model is due to a reduced ability to regulate the phosphorylation and activation of PI3-kinase, and particularly to regulate the localisation and trafficking of PIP\textsubscript{3} (phosphatidylinositol(3,4,5)-trisphosphate), an essential lipid activator of Akt, which is regulated by PINK1 and dependent on PINK1 kinase activity.

Together, our findings indicate that loss of PINK1 function in PD attenuates Akt signalling via impaired PI3-kinase/PIP\textsubscript{3} regulation, highlighting novel fault nodes of Akt signalling in PD and exposing potential targets for its treatment.
<table>
<thead>
<tr>
<th>Poster</th>
<th>First Author</th>
<th>Poster Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lindsay Tetreault</td>
<td>Is Preoperative Duration of Symptoms a Significant Predictor of Functional Outcomes in Patients Undergoing Surgery for the Treatment of Degenerative Cervical Myelopathy?</td>
</tr>
<tr>
<td>2</td>
<td>Mohamad Saab</td>
<td>Enhancing Men’s Awareness of Testicular Disorders Using Virtual Reality: The E-MAT Study</td>
</tr>
<tr>
<td>3</td>
<td>Jackie ODwyer</td>
<td>Cost Analysis of including all respiratory medicines in PCRS schemes.</td>
</tr>
<tr>
<td>4</td>
<td>Christina Dillon</td>
<td>Nutritional Habits, Physical Activity Levels, and Knowledge of Food Labels among Undergraduate University Students</td>
</tr>
<tr>
<td>6</td>
<td>Ailbhe Spillane</td>
<td>What are the physical and psychological health effects of suicide bereavement on family members? A mixed-methods study</td>
</tr>
<tr>
<td>8</td>
<td>Sarah-Louise Long</td>
<td>Probiotic potential of new Lactobacillus salivarius isolate with regards to BSH activity</td>
</tr>
<tr>
<td>9</td>
<td>Leah D’Souza</td>
<td>Students views on teaching at the anatomy and radiology interface in a digital age.</td>
</tr>
<tr>
<td>10</td>
<td>Emmy Racine</td>
<td>Participants’ Perspectives and Preferences on Clinical Trial Result Dissemination: The TRUST Thyroid Trial Experience</td>
</tr>
<tr>
<td>11</td>
<td>Dervla O’Malley</td>
<td>Vagal nerve activity is stimulated by GABA-secreting probiotics signalling across the colonic mucosal barrier.</td>
</tr>
<tr>
<td>12</td>
<td>Dervla O’Malley</td>
<td>Ghrelin enhances GLP-1 induced neuronal activation in the distal colon.</td>
</tr>
<tr>
<td>13</td>
<td>Anel Wiese</td>
<td>A Realist Synthesis of Supervisor-Trainee Interactions in Postgraduate Medical Education and Training</td>
</tr>
<tr>
<td>14</td>
<td>Indra San Lazaro Campillo</td>
<td>Ectopic pregnancy and miscarriage hospital admission in Ireland: incidence, type of management and morbidity indicators.</td>
</tr>
<tr>
<td>15</td>
<td>Karen Mention</td>
<td>CFTR Superexon Homology-Independent Targeted Integration to Correct CF-causing Variants in and Downstream of Exon 23</td>
</tr>
<tr>
<td>16</td>
<td>Eric Lucking</td>
<td>Chronic intermittent hypoxia elicits tachycardia and reduced respiratory variability in the carotid body hypoxia-insensitive guinea pig</td>
</tr>
<tr>
<td>17</td>
<td>Rebecca O’Brien</td>
<td>Ghrelin sensitises colonic myenteric neurons to the neurostimulatory effects of glucagon-like peptide-1 in Sprague Dawley and Wistar Kyoto rats</td>
</tr>
<tr>
<td>18</td>
<td>Rebecca O’Brien</td>
<td>Effects of Glucagon-Like Peptide-1 analogue, Exendin-4, in the Wistar Kyoto rat model of Irritable Bowel Syndrome.</td>
</tr>
<tr>
<td>19</td>
<td>Anja Tetzner</td>
<td>Decarboxylation of Ang-(1-7) to Ala-Ang-(1-7) leads to major changes in pharmacodynamics</td>
</tr>
<tr>
<td>20</td>
<td>Anja Tetzner</td>
<td>The AT2 receptor agonist, C21, can also stimulate Mas and MrgD receptors</td>
</tr>
<tr>
<td>Page</td>
<td>Authors</td>
<td>Title</td>
</tr>
<tr>
<td>------</td>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>21</td>
<td>Christina Fleming</td>
<td>Quantification of perioperative ctDNA levels and inflammatory markers may identify patients at risk of early recurrence in colon cancer</td>
</tr>
<tr>
<td>23</td>
<td>Marcel van de Wouw</td>
<td>The impact of the fermented milk drink kefir on physiology, immunology and behaviour.</td>
</tr>
<tr>
<td>24</td>
<td>Kim O'Brien</td>
<td>Incidence of Subsequent Stoke in Patients Attending the Rapid Access TIA Clinic in Cork University Hospital</td>
</tr>
<tr>
<td>25</td>
<td>Shauna Wallace Fitzsimons</td>
<td>An Oxytocin Feast: Novel signalling of the Oxytocin Receptor with the Ghrelin Receptor and Glucagon like Peptide 1 Receptor in Social Eating</td>
</tr>
<tr>
<td>26</td>
<td>Yensi Flores</td>
<td>Synthetic Biology In The Driving Seat Of The Bioeconomy</td>
</tr>
<tr>
<td>27</td>
<td>Joseph Murphy</td>
<td>A 3D cell culture model for candidate drug screening in Pancreatic Ductal Adenocarcinoma</td>
</tr>
<tr>
<td>28</td>
<td>Beth Brint</td>
<td>Engagement of Fas differentially regulates the production of LPS-induced pro-inflammatory cytokines and type I Interferons</td>
</tr>
<tr>
<td>29</td>
<td>Shona Cronin/Yensi Flores</td>
<td>Bacteria tumour targeting and in situ delivery of therapeutics</td>
</tr>
<tr>
<td>30</td>
<td>Beth Brint</td>
<td>Investigation of the role of IL-36 cytokines in colon cancer</td>
</tr>
<tr>
<td>31</td>
<td>Yensi Flores</td>
<td>Assembling proteins with light</td>
</tr>
<tr>
<td>33</td>
<td>Kheshwant Gill</td>
<td>Combination of electroporation delivered metabolic modulators with low-dose chemotherapy and the immune response in Osteosarcoma</td>
</tr>
<tr>
<td>34</td>
<td>Muhammad Shahzad Ali</td>
<td>Stemness induced by Electrochemotherapy in Pancreatic Adenocarcinoma</td>
</tr>
<tr>
<td>37</td>
<td>Caroline Daly</td>
<td>The increasing use of gabapentinoids in intentional drug overdose: findings from the National Self-Harm Registry Ireland, 2007-2015</td>
</tr>
<tr>
<td>38</td>
<td>Ruth McCullagh</td>
<td>Factors associated with walking in older medical inpatients</td>
</tr>
<tr>
<td>39</td>
<td>Joshua Lyte</td>
<td>Dynamic Gastrointestinal Serotonergic Responses to an Acute Stressor: Role of Host Genetics</td>
</tr>
<tr>
<td>41</td>
<td>Andrew Moore</td>
<td>The virtually mature BNP (BNP1-32) is a precursor for the more potent BNP1-30</td>
</tr>
<tr>
<td>42</td>
<td>Andrew Moore</td>
<td>Degradation of Ang-(1-7) in Different Mouse Organs</td>
</tr>
<tr>
<td>43</td>
<td>Katherine Dadswell</td>
<td>Evidence for Microcompartment-Mediated Metabolism in Urinary Tract Infection</td>
</tr>
<tr>
<td>45</td>
<td>Aoibhheann Flynn</td>
<td>Pilot project on electronic photo-triage of referrals for infantile haemangiomas</td>
</tr>
<tr>
<td>46</td>
<td>Cian Duggan</td>
<td>An exploration of the effectiveness of an educational intervention on the use of personal protective equipment in orthopaedic theatres</td>
</tr>
<tr>
<td>47</td>
<td>Mehael Fennelly</td>
<td>Real-time Monitoring of Biological Airborne Particles in the Hospital Environment</td>
</tr>
<tr>
<td>48</td>
<td>Daniel Garcia</td>
<td>Superior capsular reconstruction for treatment of irreparable rorator cuff tears: early clinical results</td>
</tr>
<tr>
<td>49</td>
<td>Aoibhheann Flynn</td>
<td>Missed opportunities for melanoma detection in secondary care</td>
</tr>
<tr>
<td>Page</td>
<td>Author</td>
<td>Title</td>
</tr>
<tr>
<td>------</td>
<td>--------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>50</td>
<td>Niall McTernan</td>
<td>The Impact of Media Reporting on Suicide: Quality of media reporting of suicide in Ireland</td>
</tr>
<tr>
<td>51</td>
<td>Michael McInerney</td>
<td>Attitudes towards an Augmented Exercise Programme in Elderly inpatients in MUH</td>
</tr>
<tr>
<td>52</td>
<td>Muhammad Asim Javaid</td>
<td>Limitations of Neuroanatomy Web-resources</td>
</tr>
<tr>
<td>53</td>
<td>Emma O’Shea</td>
<td>Respite in dementia: An evolutionary concept analysis</td>
</tr>
<tr>
<td>55</td>
<td>Anne Marie Cusack</td>
<td>The impact of breast feeding on stress, cognition and the gut microbiota in adults.</td>
</tr>
<tr>
<td>56</td>
<td>Yvonne Kiernan</td>
<td>The effects of Inflammatory Dermatological and Rheumatological conditions and their associated systemic medications on Oral Health.</td>
</tr>
<tr>
<td>57</td>
<td>Meghan Bourque</td>
<td>Incidence, associations, and impact of antibodies of undetermined significance in solid-phase technology.</td>
</tr>
<tr>
<td>58</td>
<td>Aleksandra Somogyi</td>
<td>Therapeutic targeting of impaired lysosomal flux in Alzheimer's disease</td>
</tr>
<tr>
<td>60</td>
<td>Siobhan Fo0</td>
<td>Demonstrating the potential benefit of palliative care input for people living with dementia, using case studies</td>
</tr>
<tr>
<td>61</td>
<td>Danka Kozareva</td>
<td>Absence of the neurogenesis-dependent nuclear receptor TLX induces inflammation in the hippocampus</td>
</tr>
<tr>
<td>62</td>
<td>Anne Marie Liston</td>
<td>Factors Associated with Influenza Vaccination Among Health Care Workers:A Cross-Sectional Study</td>
</tr>
<tr>
<td>63</td>
<td>Karen O’Connor</td>
<td>Bugs, Breathing and Blood Pressure: Intermittent Hypoxia Related Cardio-Respiratory Dysfunction in Rat</td>
</tr>
<tr>
<td>65</td>
<td>Dorothy Leahy</td>
<td>Profile of patients presenting to emergency departments in the Southwest of Ireland following repeated episodes of self-harm</td>
</tr>
<tr>
<td>66</td>
<td>Jack Leacy</td>
<td>USING A STANDING WORKSTATION DOES NOT ATTENUATE THE TIME-DEPENDENT DECLINE IN NEUROVASCULAR COUPLING RESPONSE MAGNITUDE</td>
</tr>
<tr>
<td>67</td>
<td>Amber Hilliard</td>
<td>Regulatory considerations for gene therapy design</td>
</tr>
<tr>
<td>68</td>
<td>Julia Samson</td>
<td>Investigating the association between long non-coding RNAs and ductal carcinoma in situ (DCIS)</td>
</tr>
<tr>
<td>69</td>
<td>Mike Stanton</td>
<td>Development of a Click Beetle&amp;nbsp;Luciferase Reporter System for Enhanced Bioluminescence Imaging of Listeria monocytogenes: Analysis in Cell Culture and Murine Infection</td>
</tr>
<tr>
<td>70</td>
<td>Anirudh Vinay Jaisimha</td>
<td>Glial-mediated clearance of extracellular autophagic-lysosomal organelles generated by cultured neurons: Relevance to Alzheimer Disease</td>
</tr>
<tr>
<td>73</td>
<td>Siobhan O'Sullivan</td>
<td>Does daily consumption of vitamin K1 from cruciferous vegetables reach the circulation?</td>
</tr>
<tr>
<td>74</td>
<td>Ruth Benson</td>
<td>The development of a Suicide and Self-Harm Observatory (SSHO) in Ireland</td>
</tr>
<tr>
<td>75</td>
<td>Venkata Vamsi Bharadwaj Yallapragada</td>
<td>In situ bacterial production of therapeutic antibody fragments</td>
</tr>
<tr>
<td>76</td>
<td>Alice O’Brien</td>
<td>Limitations in the use of Iron Indices as Markers for Iron Overload</td>
</tr>
<tr>
<td>Page</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>77</td>
<td>Isolation of Virus-Free Antigen Binding Fragments (VF-FAbs) from Antibody-Associated Hepatitis C Virus</td>
<td>Nicole Walsh</td>
</tr>
<tr>
<td>78</td>
<td>Non-receptor tyrosine kinase FER enhances Insulin-like Growth Factor-1 Receptor activation to promote an aggressive cancer phenotype.</td>
<td>Leonie Rieger</td>
</tr>
<tr>
<td>80</td>
<td>Expression of p40 versus p63 in Cutaneous Squamous Cell Carcinoma and Cutaneous Spindle Cell Malignancies</td>
<td>Cynthia Heffron</td>
</tr>
<tr>
<td>82</td>
<td>Knowledge, attitudes and beliefs of parents regarding adolescent human papillomavirus (HPV) vaccination: a systematic review and meta-ethnographic synthesis of the qualitative literature.</td>
<td>Sarah Marshall</td>
</tr>
<tr>
<td>84</td>
<td>Markers of apoptosis and autophagy are predictive of survival in oesophageal adenocarcinoma.</td>
<td>Tracey O'Donovan</td>
</tr>
<tr>
<td>85</td>
<td>High Concordance of BRAF Mutational Status by Molecular and Immunohistochemical Methods between Melanoma Primary and Metastases</td>
<td>Cynthia Heffron</td>
</tr>
<tr>
<td>86</td>
<td>The primary cilium in the CNS: an organelle of stress-related psychiatric disorders and antidepressant action?</td>
<td>Valentina Novelli</td>
</tr>
<tr>
<td>87</td>
<td>Role of specific sub-regions along the longitudinal axis of the hippocampus in the behavioural responses to chronic stress</td>
<td>Brunno R. Levone</td>
</tr>
<tr>
<td>88</td>
<td>A marker panel consisting of LC3B, TRIM24 and Caveolin-1 predicts survival of oesophageal adenocarcinoma patients</td>
<td>Tracey O'Donovan</td>
</tr>
<tr>
<td>89</td>
<td>Investigating a role for autophagy in ovarian cancer chemoresistance</td>
<td>Jennifer Quinn</td>
</tr>
<tr>
<td>91</td>
<td>Psychotropic drugs modulate the gut microbiota in vivo</td>
<td>Sofia Cussotto</td>
</tr>
<tr>
<td>92</td>
<td>The Who, What, and Why of Drug Discovery</td>
<td>Glenn Hogan</td>
</tr>
<tr>
<td>93</td>
<td>Older Peoples &amp; Experiences of Attending Falls Risk Assessment Clinics in Primary Care</td>
<td>Emmy Racine</td>
</tr>
<tr>
<td>95</td>
<td>In silico design of synthetic therapeutic antibody fragments</td>
<td>Venkata Vamsi Bharadwaj Yallapragada</td>
</tr>
<tr>
<td>96</td>
<td>Gut microbiota manipulation through caesarean section delivery alters hippocampalsynaptic response</td>
<td>Rory O'Connor</td>
</tr>
<tr>
<td>97</td>
<td>Developing a Core Outcome Set of Infant Feeding Outcomes for Obesity Prevention Interventions</td>
<td>Karen Matvienko-Sikar</td>
</tr>
<tr>
<td>98</td>
<td>The CHErIsH Study: Developing primary care based pilot infant feeding intervention to prevent childhood obesity</td>
<td>Karen Matvienko-Sikar</td>
</tr>
<tr>
<td>99</td>
<td>Prevalence of Bendopnea in Systolic Heart Failure Patients</td>
<td>Cara Pray</td>
</tr>
<tr>
<td>100</td>
<td>Chronic intermittent hypoxia induced respiratory muscle dysfunction in adult male mice: a role for NADPH oxidase</td>
<td>Sarah Drummond</td>
</tr>
<tr>
<td>101</td>
<td>Analysis of comparable home / clinic blood pressure readings in the LEANBH population</td>
<td>Eoin Roche</td>
</tr>
</tbody>
</table>
Is Preoperative Duration of Symptoms a Significant Predictor of Functional Outcomes in Patients Undergoing Surgery for the Treatment of Degenerative Cervical Myelopathy?

L Tetreault1,2, JR Wilson1,3, MRN Kotter1,4, P Cote5, A Nouri1, B Kopjar6, PM Arnold7, MG Fehlings1

1Division of Neurosurgery, Toronto Western Hospital, Toronto, Canada
2Graduate Entry Medicine, University College Cork, Cork, Ireland
3Division of Neurosurgery, St. Michael's Hospital, Toronto, Canada
4Division of Neurosurgery, Cambridge University, Cambridge, United Kingdom
5Faculty of Health Sciences, University of Ontario Institute of Technology, Oshawa, Canada
6School of Public Health, University of Washington, Seattle, United States of America
7Department of Neurosurgery, University of Kansas, Kansas City, United States of America

Background: Preoperative duration of symptoms may significantly impact outcomes in patients treated surgically for degenerative cervical myelopathy (DCM)

Objective: This observational study aims to analyze whether a longer duration of symptoms is associated with poor surgical outcomes in patients with DCM.

Methods: Patients with DCM were prospectively enrolled in either the CSM-North America or International study at 12 sites (n=350). Postoperative functional impairment was evaluated at 1-year using the modified Japanese Orthopaedic Association (mJOA). Change scores between baseline and 1-year were computed for the mJOA. Duration of symptoms was dichotomized into a “short” and “long” group at several cut-offs. A mixed model analytic approach was used to evaluate differences in change scores on the mJOA between duration groups in 1-month increments, while controlling for confounders. This analysis was repeated for subgroups of patients with mild (mJOA≥15), moderate (mJOA=12-14) and severe (mJOA<12) myelopathy.

Results: Our cohort consisted of 201 men and 149 women, with a mean duration of symptoms of 25.71±36.68 months. Patients with a duration of symptoms shorter than 4 months had significantly better functional outcomes based on the mJOA than patients with a longer duration of symptoms (>4 months). When stratifying by myelopathy severity, we were unable to identify an appropriate cut-off for patients with mild myelopathy. In patients with moderate disease, however, each 1-month delay in surgery had a significant impact on clinical outcomes.
Conclusions: Patients who are operated on within 4 months of symptom presentation have better mJOA outcomes than those treated after this 4-month cut-off.

P2

Enhancing Men's Awareness of Testicular Disorders Using Virtual Reality: The E-MAT Study

MM Saab1, M Landers1, E Cooke2, D Murphy2, M Davoren3, J Hegarty1

1School of Nursing and Midwifery, University College Cork, Cork, Ireland
2Computer Science, University College Cork, Cork, Ireland
3Epidemiology & Public Health, University College Cork, Cork, Ireland

Background

Men’s awareness of testicular disorders is lacking and their intention to seek help for scrotal symptoms is low. Few studies promoted awareness of testicular disorders with none using innovative technologies. The aim of this study was to enhance men’s testicular awareness via an intervention delivered using virtual reality and underpinned by a novel theoretical framework.

Methods

A one-group pre- and post-test design was used. Men (n=53) aged between 18 and 50 years were recruited using non-probability sampling and were asked to play a 3-level educational game using a virtual reality headset, a controller, and headphones with voiceover. Knowledge, awareness, perceived risk, implementation intentions, help-seeking intentions, and behaviour were measured at three time points: baseline, immediately post-test, and one month post-test. Data were analysed using descriptive and inferential statistics including repeated measures.

Results

Men’s knowledge and awareness of the normal testes and testicular symptoms and diseases; intentions to examine their testes; intentions to seek help for testicular symptoms; and behaviours pertaining to feeling their testes increased over time. This increase was found to be statistically significant. Men who intended to feel their testes and to advise other men to do the same at baseline reported having done that one month post-test. In contrast, men’s perceived risk for developing a testicular disorder was low at baseline and did not increase over time.

Conclusion

The intervention proved successful in enhancing men’s testicular awareness, implementation intentions, help-seeking intentions, and behaviours. The plan is to
conduct a randomised controlled trial and to test the intervention using a larger sample size.

P3

Cost Analysis of including all respiratory medicines in PCRS schemes.

J ODwyer, A Murphy

Department of Economics, Cork University Business School, University College Cork, Cork, Ireland

Aim: This study estimates the additional cost to the State to pay for all respiratory medicines through the Primary Care Reimbursement Service (PCRS) schemes, reducing cost barriers to medication as a complement to existing chronic disease management programmes. Previous literature found higher medication adherence rates amongst medical card patients (GMS) than those that had to pay or co-pay themselves [1].

Method: A review of medication expenditure on the PCRS schemes from 2005-2015. Data on all medicines sold into and out of pharmacies [2] was used to estimate the proportion to PCRS schemes or private. Scenario analyses were conducted to estimate what the cost to the State would be to provide funding for all respiratory medicines.

Results: Findings showed that respiratory medicines have been less than 10% of total PCRS medicines expenditure. The largest portion of the respiratory medicines expenditure is allocated to ‘Drugs for Obstructive Pulmonary Disorder (OPD)’, ranging from 90% in 2005 to 69% in 2015. 87% of drugs to treat OPD are dispensed publically and 13% privately. A scenario analysis estimated that the extra cost to the State ranged between €20.2m to €33.8m.

Conclusions: Respiratory disease, is included in the Irish Governments chronic disease management programme. This aims to deliver optimal care in the most appropriate setting so as to improve health outcomes and quality of life. Medication adherence is imperative to achieving these aims. Reducing cost barriers, as a complement to existing initiatives could improve medicine adherence thereby improving the effectiveness of disease management and patient outcomes.

References.
Nutritional Habits, Physical Activity Levels, and Knowledge of Food Labels among Undergraduate University Students

A O'Sullivan¹, L Delaney¹, M Smiddy¹, CB Dillon²

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

Background: Overweight and obesity (OVOB) are associated with increased morbidity and mortality. Physical inactivity, poor diet and lack of knowledge and use of food labels are associated with OVOB. The time students spend at university is seen as an influential period for developing poor lifestyle behaviours and thus an important period for prevention.

Objective: To examine the association between dietary habits, physical activity (PA) levels, knowledge and use of food labelling and OVOB status among university students.

Methodology: Seven-hundred and six undergraduate students (66% females) completed an online questionnaire measuring Body Mass Index, dietary habits, PA levels and knowledge and use of food labels. Descriptive statistics and regression analyses examined the association between PA, dietary habits and, food label use and knowledge on OVOB status.

Results: Thirty percent of the student population were overweight or obese, female (59%), P=0.009. Analyses observed only dietary habits (fizzy drinks and meat consumption) to be significantly related to OVOB in female students. Those who rarely consumed fizzy drinks were 70% less likely to be OVOB (OR: 0.29, 95% CI 0.14-0.58) compared to those who consumed them 3-7 times per week. Those who consumed unprocessed (OR:6.43, 95% CI 1.49-27.85) and processed meats (OR: 2.59, 95% CI 1.25-5.38 and OR: 2.54, 95% CI 1.05-6.15) were more likely to be OVOB compared to those who rarely consumed them.

Conclusion: Findings suggest the need for gender-specific dietary related strategies designed to improve lifestyle behaviours of students with a focus on female students.

T O'Donnell, Z Di Blasi, M Murphy

School of Applied Psychology, University College Cork, Cork, Ireland

Overview: Many psychological mechanisms such as expectancy, enhanced interaction and cognitive reappraisal (CRA) have been shown to enhance placebo responses and reduce affective impact. The aim of this study is to examine whether context effects impact stress, more than commercially available treatments such as Bach flower remedies.

Method: 2X2 double-blind placebo RCT design was used to evaluate the effects of ‘Rescue Remedy’ versus placebo in stress reactivity and recovery, and to examine the role of enhanced consultation and CRA. 36 participants were randomised to receive Bach flower remedy (n=20) or Placebo (n=16), then further randomised to receive a) Enhanced consultation with placebo priming and stress CRA, OR b) Standard consultation.

Participants were subsequently subjected to the Sing-a-song stress test. Heart rate reactivity and recovery were monitored to evaluate physiological stress.

Results: A hypothesis that Rescue remedy would have no effect above that of a placebo was supported. A series of ANOVAs found no significant difference between placebo and Rescue Remedy groups’ HR reactivity and recovery. A hypothesis that enhanced consultation style would significantly impact on stress reactivity and recovery was partially supported as there were significant results for HR reactivity but not recovery. Perceived treatment was also found to be a unique predicting factor for HR reactivity.

Conclusions: Major findings from this study were supported by current literature. However the lack of significant results for HR recovery was not, suggesting a flaw in the methodology. Future research would be advised to use a larger more diverse sample.

A second wave of recruitment is underway, aimed at increasing participant n and introducing a no-treatment group.
What are the physical and psychological health effects of suicide bereavement on family members? A mixed-methods study

A Spillane¹, ², K Matvienko-Sikar¹, C Larkin³, P Corcoran², ⁴, E Arensman¹, ²

¹Department of Epidemiology and Public Health, University College Cork, Cork, Ireland
²National Suicide Research Foundation, University College Cork, Cork, Ireland
³Department of Emergency Medicine, University of Massachusetts Medical School, Worcester, United States
⁴Department of Obstetrics and Gynaecology, Cork University Maternity Hospital, Cork, Ireland

Background: Quantitative research has highlighted adverse mental health outcomes of suicide bereavement, including heightened risk of suicide and attempted suicide. However, mixed-methods research specifically focussing on the impact of suicide bereavement on family members’ physical and psychological health is scarce.

Methods: A mixed-methods study was conducted, using qualitative interviews and quantitative self-report measures of depression, anxiety and stress (DASS-21). Consecutive suicide cases and next-of-kin were identified by examining coroner’s records in Cork City and County. Eighteen family members bereaved by suicide took part in a qualitative interview. They were recruited from the Suicide Support and Information System: A Case-Control Study (SSIS-ACE) where family members bereaved by suicide (n = 33) completed structured measures of their wellbeing (DASS-21).

Results: Qualitative findings indicated four superordinate themes in relation to experiences following suicide bereavement: (1) immediate grief reactions; (2) enduring physical, psychological and psychosomatic difficulties; (3) range of support needs required and its influencers; and (4) reconstructing life after deceased’s suicide. Initial feelings of guilt, blame, shame and anger often manifested in enduring physical, psychological and psychosomatic difficulties. Quantitative results indicated that the proportion of respondents above the DASS-21 cut-offs respectively were 24% for depression, 18% for anxiety and 27% for stress.

Conclusions: The effects of suicide bereavement are wide-ranging, including high levels of stress, depression, anxiety, and physical health difficulties. Greater awareness amongst healthcare professionals regarding these adverse health difficulties experienced by those
bereaved by suicide is essential. Pro-actively facilitating support for this group could help to reduce the negative health sequelae.

P8

Probiotic potential of new *Lactobacillus salivarius* isolate with regards to BSH activity

SL Long¹,²,⁴, F Shanahan¹, CGM Gahan¹,²,³, SA Joyce¹,⁴

¹APC Microbiome Institute, University College Cork, Cork, Ireland
²School of Microbiology, University College Cork, Cork, Ireland
³School of Pharmacy, University College Cork, Cork, Ireland
⁴School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland

*Lactobacillus* species are commonly applied as probiotics with the prerequisite that they can metabolise bile acid (BA). This metabolic activity is dependent on the presence of bile salt hydrolase (BSH) enzymes which initiate the gateway reaction for BA metabolism in the gut by commensal microbes. These bile altering microbes govern the overall BA composition of the host which has been shown to be altered in a variety of disease states such as IBD.

This study describes a new isolate and subspecies of *L. salivarius* of porcine origin. This strain was characterised genetically by *de novo* sequencing to detect the presence of BSH enzymes. UPLC-MS determined the *in vitro* activity and range of these BSH enzymes following incubation with 32 individual BAs. This *L. salivarius* strain was also assessed for EFSA characteristics and studied *in-vitro* (gut simulation model) and *in-vivo* (mouse model) to examine its probiotic potential with an emphasis of the alteration of the host BA pool.

Our new BSH positive strain of *L. salivarius* contained three distinct BSH sequences. Their collective activity revealed that these enzymes are active in deconjugation with preference towards a number of specific BA to yield a unique profile for this isolate. Gut simulation assays, EFSA and *in-vivo* assessment indicate this strain’s ability to influence the composition of the host BA pool under different diet conditions.

We question whether strains with fully characterised BSH activity such as our *L. salivarius* can be applied as a probiotic to ameliorate effects of specific BA alterations seen in certain disease conditions.
Students views on teaching at the anatomy and radiology interface in a digital age. 
LA D'Souza¹, GW O’Keeffe²

¹School of Medicine, University College Cork, Cork, Ireland  
²Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

BACKGROUND: As image guidance medicine takes precedence in clinical practice, educators continue to search for cost-effective and resource efficient approaches to better integrate medical imaging and radiographic anatomy into the undergraduate curriculum.

AIMS: Here we carried out a scoping study to identify students’ perceptions of the integration of radiology and anatomy, and assessed students’ willingness to participate in an on-line collaborative, peer-facilitated platform being developed to facilitate their greater integration.

MATERIALS AND METHODS: An online questionnaire was distributed to first year medical students (n=78) during the 2016-2017 academic year. The survey included questions designed to collect student demographic information, information on prior experiences in anatomy and radiology, and preferred methods for learning anatomy and radiology.

RESULTS: Sixty-four surveys were returned (82.1% response rate). 69% of students reported they had no previous exposure to reading radiographs prior to enrolling in medical school. When asked whether they felt they received adequate exposure to radiology in medical school, over half of respondents provided negative responses (“Strongly disagree or disagree”) with a mean Likert scale score of 2.47 ± 0.22. The majority of students were keen to participate in a peer-led collaborative online academic learning platform in radiographic anatomy.

CONCLUSION: These findings provide a better understanding of students’ perceptions of the current approach to teaching medical imaging and support the development of a more tailored approach to delivering adequate education in a cost-effective and resource efficient manner through a on-line, peer-lead blended learning platform.

Keywords: Medical imaging, Medical education, Anatomy education, Blended learning
Participants’ Perspectives and Preferences on Clinical Trial Result Dissemination: The TRUST Thyroid Trial Experience

E RACINE1, C HURLEY 1, A CHEUNG1, C SINNOTT3, K MATVIENKO-SIKAR1, WH SMITHSON2, P KEARNEY1

1Department of Epidemiology and Public Health, University College Cork, Cork, Ireland
2Department of General Practice, University College Cork, Cork, Ireland
3Department of Public Health and Primary Care, University of Cambridge, Cambridge, U.K

Background
The results of clinical trials are not traditionally disseminated to clinical trial participants and little is known about the most appropriate methods of doing so. The Thyroid Hormone Replacement for Subclinical Hypothyroidism Trial (TRUST) was a multicentre trial which tested the efficacy of thyroxine replacement in subclinical hypothyroidism in older adults (≥65 years). Our aim was to use a Public and Patient Involvement (PPI) approach to identify, develop and evaluate a patient-preferred method of receiving the results of the TRUST Thyroid Trial.

Methods
Using a mixed methods approach, an intervention study was undertaken at the Irish TRUST site. There were three phases of the study. (1) A PPI approach was used to develop a patient-preferred result method. (2) Irish TRUST participants (n=101) were randomised into the intervention (PPI method) and comparison groups (standard method). (3) All participants were sent a questionnaire. The primary outcome was difference in understanding of results between the two groups.

Results
(1) A results letter was developed containing a 2-3 page summary of the trial, condition, treatment and overall results. (2) All randomised participants received the results of the trial (n=101). (3) The response rate was 66% (n=67). There were no differences in patient understanding between the intervention and comparison groups.

Conclusions
While this study found that PPI has no real impact on patient understanding of trial results, it provides empirical evidence on participants’ perspectives and preferences of clinical trial result dissemination and provides a template for enhancing patient and public involvement in research.
Vagal nerve activity is stimulated by GABA-secreting probiotics signalling across the colonic mucosal barrier.

MM Buckley\textsuperscript{1,2}, G O'Driscoll\textsuperscript{2}, C Stanton\textsuperscript{1,3}, D O'Malley\textsuperscript{1,2}

\textsuperscript{1}APC Microbiome Institute, UCC, Cork, Ireland
\textsuperscript{2}Department of Physiology, UCC, Cork, Ireland \textsuperscript{3}Teagasc Food Research Centre, Moorepark, Cork, Ireland

The vagus nerve appears to be a key mediator in the bidirectional neuro-hormonal communication system between the central nervous system, the gastrointestinal tract and now, the luminal microbiome. However, the mechanisms by which luminal microbes signal across an intact epithelium to the afferent nerve endings is unknown. In this study we have attempted to unravel the mechanisms by which a GABA-producing putative probiotic, Lactobacillus brevis DPC 6108 communicates with the host nervous system. Calcium imaging of colonic submucosal neurons from adult male Sprague Dawley rats and recordings of vagal nerve activity in response to colonic mucosal stimulation by secretions from Lactobacillus brevis DPC 6108 (supernatants) were carried out. Mucosal exposure to probiotic supernatants induced a large increase in intracellular calcium in submucosal neurons, which was attenuated by bicuculline, a GABA\textsubscript{A} receptor antagonist (n=27, p<0.001) and to a lesser extent by the GABA\textsubscript{B} receptor antagonist, phaclofen (n=19, p<0.05). Application of supernatants to the distal colonic mucosa also elicited a robust increase in vagal nerve firing (n=4, p<0.001), which was suppressed by bicuculline, (p<0.001) and phaclofen (p<0.05). These data demonstrate that secretions from Lactobacillus brevis DPC 6108 signal across the intact epithelium to stimulate submucosal neurons and vagal nerve afferents. Both GABA\textsubscript{A} and GABA\textsubscript{B} receptors are necessary for this probiotic to communicate with the host nervous system.
Ghrelin enhances GLP-1 induced neuronal activation in the distal colon.

MM Buckley\textsuperscript{1,2}, R O'Brien\textsuperscript{2}, D O'Malley\textsuperscript{1,2}

\textsuperscript{1}APC Microbiome Institute, UCC, Cork, Ireland
\textsuperscript{2}Department of Physiology, UCC, Cork, Ireland

Irritable Bowel Syndrome (IBS) is a chronic condition characterised by bouts of cramping, abdominal pain, constipation and/or diarrhoea, with many patients complaining of post-prandial symptom exacerbation. As the orexigenic hormone, ghrelin peaks prior to a meal and the gut hormone, glucagon like peptide-1 (GLP-1) food ingestion, we sought to investigate their possible role in post-prandial IBS symptom exacerbation. Colonic myenteric plexus tissue was prepared from adult male Sprague Dawley (SD) rat controls and the Wistar Kyoto (WKY) rat model of IBS. Calcium imaging was carried out on myenteric neurons and nerve activity was recorded from the vagus to determine if ghrelin sensitises neurons to the neurostimulatory effects of GLP-1. Ghrelin potentiated the GLP-1-induced increase in intracellular calcium in myenteric neurons of both SD (n=24, p<0.01) and WKY (n=40, p<0.001) rats. Exposure of colonic myenteric neurons to ghrelin prior to GLP-1 also enhanced vagal firing in both rat species (SD: p<0.001, WKY: p<0.01). Prior exposure to ghrelin, as may occur during the ghrelin peak prior to food ingestion, appears to sensitise colonic myenteric neurons to the neurostimulatory effects of GLP-1. Moreover, sensitisation of myenteric neurons by exposure to ghrelin enhances the gut-to-brain signalling via the vagus nerve. Despite alterations in gastrointestinal function in WKY rats, this mechanism is similar to the control SD rat.
A Realist Synthesis of Supervisor-Trainee Interactions in Postgraduate Medical Education and Training

A Wiese¹, C Kilty¹, B Maher¹, C Bergin², M Horgan¹, D Bennett¹

¹Medical Education Unit, University College Cork, Cork, Ireland
²School of Medicine, Trinity College Dublin, Dublin, Ireland

Background: Workplace learning is recognised as being at the heart of postgraduate medical training. The aim of this study was to synthesise the evidence relating to workplace learning in postgraduate medical education to address the question ‘What works, under what circumstances and for whom?’

Method: A realist synthesis/review of the literature was conducted in line with the RAMESES guidelines. A realist review is an interpretive, theory-driven, narrative summary of the literature and aims to develop a theoretical framework describing Context-Mechanism-Outcome (CMO) configurations of how, why and when postgraduate medical training is effective.

Results: Findings involve mechanisms that generate learning within the framework of the trainee-supervisor relationship such as observation, modelling, dialogue, feedback and entrustment. Constraints in the clinical setting modifies how mechanisms generate learning outcomes and include organisational culture, trainee-, supervisor- and patient-related factors, EWTD, the structure of training programs, and work load.

Conclusions: This study utilised published literature, programme and substantive theories of workplace learning to describe context, mechanism and outcome configurations. These causal mechanisms in postgraduate medical education can direct the design of high quality learning environments that are effective for learning and create satisfactory working conditions for doctors in training. Clinical learning environments, the context, shapes the development of the doctors who learn and work within it. Those tasked with the design and delivery of postgraduate medical education need to understand the relationship between the processes of medical workplace learning and these contextual elements to optimise conditions for learning.
Ectopic pregnancy and miscarriage hospital admission in Ireland: incidence, type of management and morbidity indicators.

I San Lazaro Campillo, S Meaney, K O'Donoghue, P Corcoran

1Pregnancy Loss Research Group, Department of Obstetrics and Gynaecology, University College Cork, Cork, Ireland
2National Perinatal Epidemiology Centre, University College Cork, Cork, Ireland
3The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork, Ireland
4Department of Epidemiology and Public Health, University College Cork, Cork, Ireland

Ectopic pregnancy (EP) and miscarriage are among the most common obstetric causes of maternal morbidity early in pregnancy. However, data concerning non-fatal complications among hospitalisations for both conditions are lacking. The aim was to explore trends in incidence rates and to estimate morbidity associated with hospitalisations for EP and miscarriage in the Republic of Ireland (ROI). A population-based study of all inpatient admissions for EP and miscarriage in all maternity hospital settings from January 2005 to December 2015 using inpatient data from the Hospital In-Patient Enquiry (HIPE) database. Overall, a rate of 14.9/1000 deliveries for EP and a rate of 70/1000 deliveries for miscarriage were observed. Over the 11-year period, rates for women with EP increased and rates for miscarriage decreased. Among the 10,994 hospitalisations for EP, 55% (n=551) had a blood transfusion (BT) and 34.9% (n=3,837) had an extended length of stay (LOS) over 2 days. Compared to women who underwent expectant treatment for EP, those who underwent salpingectomy had three times the BT rate. Among the 51,757 hospitalisations for miscarriage, 1.3% (n=685) had a BT and 3% (n=1,565) had a LOS over 2 days. Women who were managed surgically had three times the rate of BT compared to expectant management. Women who had a late miscarriage were almost four times more likely to have a BT than those who had early miscarriage. In conclusion, EP and miscarriage had divergent hospitalisations rates. Surgical treatment and late miscarriage might increase rates of morbidity indicators among inpatients admissions.
P15

CFTR Superexon Homology-Independent Targeted Integration to Correct CF-causing Variants in and Downstream of Exon 23

K Mention¹, K Cavusoglu-Doran¹, D Sanz¹, M Scallan², P Harrison¹

¹Physiology, University College Cork, Cork, Ireland
²Microbiology, University College Cork, Cork, Ireland

Gene editing of individual Cystic Fibrosis (CF)-causing variants by homology-directed repair is precise, but the efficiency is rarely above 1% of transfected cells without drug selection. Moreover, editing each of the 280 known CF-causing mutations individually is not a feasible therapeutic approach. To address this, we and others successfully incorporated a CF Superexon¹¹⁻²⁷ construct into the Cystic Fibrosis transmembrane conductance regulator (CFTR) gene using Zinc-Finger Nucleases and Cas9 but efficiency was even lower.

Here we describe the efficient incorporation of a CF Superexon²³⁻²⁷ construct into the CFTR gene using homology-independent targeted integration (HITI), a recently described technique to increase stable transgene incorporation. The major advantage of HITI is that if the insert is integrated in the wrong orientation, the gRNAs used will excise the insert allowing a subsequent attempt for a correct integration without the need for additional manipulation.

We have designed and synthesized a 1.7kb CF Superexon from exon 23-27 fused to an mCherry reporter gene with a linker GT2A. The construct is designed to be incorporated into intron 22 using Cas9 gRNAs previously validated in our lab for this region. Successful integration of the CF Superexon²³⁻²⁷-2A-mCherry construct should result in a wild-type mRNA expressed under the control of the endogenous CFTR promoter.

Thus, with a single Cas9 gRNA and one relatively small donor plasmid, we expect a correction of ~5% of all CF-causing variants including the currently non-druggable W1282X and N1303K variants.
Chronic intermittent hypoxia elicits tachycardia and reduced respiratory variability in the carotid body hypoxia-insensitive guinea pig

EF Lucking¹, KM O’Connor¹,²,³, KD O’Halloran¹,³

¹Physiology, University College Cork, Cork, Ireland
²Anatomy and Neuroscience, University College Cork, Cork, Ireland
³APC Microbiome Institute, University College Cork, Cork, Ireland

There is general consensus that carotid body (CB) sensitization is pivotal in the development of chronic intermittent hypoxia (CIH)-induced breathing instability and hypertension. We sought to determine if exposure to CIH adversely affects cardiorespiratory control in guinea-pigs, a species with hypoxia-insensitive CBs.

Adult Dunkin-Hartley male guinea pigs were exposed to repetitive cycles of hypoxia (FiO₂=0.065 nadir; 5minutes) and normoxia (FiO₂=0.21; 5minutes) for 8hours/day for 12days. Sham animals were constantly exposed to room air. Conscious breathing was assessed using whole-body plethysmography and under urethane anaesthesia (1.5g/kg i.p.) cardiorespiratory challenges were performed.

Baseline ventilation was similar in CIH and sham animals; however, the hypoxic ventilatory response was blunted and breathing variability was reduced in CIH exposed animals compared to sham animals. Baseline mean arterial pressure was unaffected by CIH exposure; nevertheless, a tachycardia was evident in CIH animals compared with sham controls. Cardiovascular responses to chemostimulation challenges (hypoxia, hypercapnia, asphyxia, sodium cyanide 200µg/kg i.v.) were overall equivalent between groups. β-adrenoceptor blockade (propranolol; 2mg/kg i.v.) produced a significantly blunted hypotensive response in CIH animals compared with sham animals, as well as an enhanced bradycardic response.

This study suggests that CB plasticity is obligatory for the development of CIH-induced hypertension. However, CIH exposure did induce modest aberrant cardiorespiratory control in the guinea-pig, presumably through actions independent of the CBs. Baseline tachycardia and an enhanced β-block induced bradycardia are suggestive of sympathetic nervous system hyperactivity at the level of the cardiac branch. We hypothesise CB-independent CIH-induced oxidative stress manifests in the cardiorespiratory control centres of the brainstem.
Ghrelin sensitises colonic myenteric neurons to the neurostimulatory effects of glucagon-like peptide-1 in Sprague Dawley and Wistar Kyoto rats

R O’Brien¹, MM Buckley¹,², D O’Malley¹,²

¹Department of Physiology, University College of Cork, Cork, Ireland
²APC Microbiome Institute, University College of Cork, Cork, Ireland

Irritable Bowel Syndrome (IBS) is a common functional bowel disorder affecting approximately 10-20% of the population with many experiencing post-prandial exacerbation of symptoms. Although IBS pathophysiology remains elusive, dysfunctional endocrine signalling has been implicated. Ghrelin is an orexigenic hormone which peaks prior to food ingestion. Glucagon-like peptide-1 (GLP-1) is secreted by L-cells in the mucosa of the small and large intestine in response to the arrival of nutrients. Previous studies have shown that ghrelin directly primes L-cells to secrete GLP-1 and increases GLP-1 release (Gagnon et al., 2014). The aims of this study were to investigate if ghrelin sensitises colonic enteric neurons for GLP-1 mediated signalling in two animal models; Sprague Dawley (control) and Wistar Kyoto (stress model of IBS).

Immunofluorescence was used to stain for ghrelin and GLP-1 receptors. Colonic motility was assessed in organ baths, using SD and WKY colonic segments, in response to a GLP-1 mimetic before and after ghrelin stimulation.

Ghrelin and GLP-1 receptors were expressed in discrete co-localised clusters in myenteric neurons. GLP-1 reduced contractile activity in both SD and WKY rat colons. However, this response was potentiated by prior exposure to ghrelin in both circular and longitudinal muscle in Sprague Dawley ((p=0.0116), (p=0.0093), respectively) and Wistar Kyoto ((p=0.0129), (p=0.0006), respectively) rat colonic segments.

Ghrelin sensitises the colon to GLP-1-evoked contractile activity. Although similar mechanisms of action were evidence in both species, the baseline contractile activity was aberrant in WKY rats.
Effects of Glucagon-Like Peptide-1 analogue, Exendin-4, in the Wistar Kyoto rat model of Irritable Bowel Syndrome.

R O'Brien¹, MM Buckley¹,², D O'Malley¹,²

¹Department of Physiology, University College of Cork, Ireland
²APC Microbiome institute, University College of Cork, Ireland

Irritable Bowel Syndrome (IBS) is a common functional bowel disorder affecting approximately 10-20% of the population. Symptoms include abdominal pain, altered bowel habit and bloating. The incretin hormone, glucagon-like peptide-1 (GLP-1) has reported anti-spasmodic and pain relieving effects in IBS patients. We assessed the effects of the GLP-1 mimetic, exendin-4 (Ex4), on IBS-like symptoms in the Wistar Kyoto (WKY) rat model of IBS. Male WKY rats received an intraperitoneal (IP) injection of Ex-4 (1.0mg/kg) or Ex-4 with anti-IL-6 receptor monoclonal antibodies (0.5mg/kg) over two weeks. Stress-induced defecation was assessed using open field arena and visceral pain sensitivity was assessed using colorectal distension (CRD). Inflammatory markers in plasma samples from each animal were examined using an ELISA bio-assay. Ex-4 treated WKY rats exhibited decreased stress-induced defecation (p<0.001) and decreased numbers of pain responses (p<0.05) during CRD as compared to saline-treated WKY rats. WKY rats receiving Ex-4 and xIL-6R entered the inner exposed circle of the open field arena fewer times than untreated WKY rats (p<0.05). Plasma analysis demonstrated that Ex-4 treated WKY rats had decreased circulating IL-2 (p<0.05) and increased IL-10 (p<0.05) in comparison to control WKY rats. Peripheral administration of a GLP-1 mimetic has beneficial effects on bowel symptoms in the WKY rat model of IBS, which is likely to be through a peripheral effects. The findings support a potential therapeutic role for GLP-1 in the treatment of visceral pain and altered bowel habit in IBS.

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Decarboxylation of Ang-(1-7) to Ala1-Ang-(1-7) leads to major changes in pharmacodynamics

A Tetzner1, M Naughton1, K Gebolys1, E Sala2, O Villacañas2, T Walther1,3,4

1Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland
2Intelligent Pharma, Barcelona, Spain
3Departments Obstetrics and Paediatric Surgery, University of Leipzig, Leipzig, Leipzig, Germany
4Institute of Medical Biochemistry and Molecular Biology, University Medicine Greifswald, Greifswald, Germany

Within the renin-angiotensin system, angiotensin (Ang)-(1-7) is cardiovascular protective, stimulates regeneration, and opposes the often detrimental effects of Ang II. We identified two receptors for the heptapeptide; the G protein-coupled receptors Mas and MrgD. Recently, a decarboxylated form of Ang-(1-7), Ala1-Ang-(1-7) (Alamandine), has been described as having similar vasorelaxant effects as Ang-(1-7), but distinctively stimulating the MrgD receptor. The aim of this study was to elucidate the consequences of the lack of the carboxyl group in amino acid one on intracellular signalling, to discover the receptor fingerprint for Ala1-Ang-(1-7), and to characterize the consequences for pharmacodynamics. Ala1-Ang-(1-7) elevated cAMP concentrations in primary endothelial and mesangial cells. However, the dose-response curves clearly discriminated from the curves generated with Ang-(1-7), with a much lower EC50 and a bell-shape curve for Ala1-Ang-(1-7). We provided pharmacological proof that both, Mas and MrgD, are functional receptors for Ala1-Ang-(1-7). Consequently, the heptapeptide failed to increase cAMP concentration in primary mesangial cells with genetic deficiency in both receptors. As for Ang-(1-7), the AT2 blocker PD123319 also blocked the Ala1-Ang-(1-7) effects on Mas and MrgD receptors and also, in primary cells. The very distinct dose-response curves for both heptapeptides could be explained by in silico modelling, electrostatic potential calculations, and an involvement of G alpha i for higher concentrations of Ala1-Ang-(1-7). Our results identify Ala1-Ang-(1-7) as a peptide with specific pharmacodynamic properties and build the basis for the design of more potent and efficient Ang-(1-7) analogues for therapeutic interventions in a rapidly growing number of diseases.
The AT2 receptor agonist, C21, can also stimulate Mas and MrgD receptors

A Tetzner¹, M Naughton¹, K Gebolys¹, E Sala², O Villacañas², T Walther¹,³

¹Dept. Pharmacology and Therapeutics, School of Medicine and School of Pharmacy, University College Cork (UCC), Cork, Ireland
²Intelligent Pharma, Barcelona, Spain
³Institute of Medical Biochemistry and Molecular Biology, University Medicine Greifswald, Greifswald, Germany.

It is well accepted that Compound 21 (C21) is a highly selective non-peptide angiotensin AT2 receptor agonist. C21 as well as angiotensin (Ang)-(1-7) have cardiovascular protective effects and are opponents of the often detrimental Ang II within the renin-angiotensin system. Since the chemical structure of C21 is similar to the Mas receptor specific non-peptidic agonist AVE0991, and we could recently show that the AT2 receptor blocker, PD123.319, can also block the effects of Ang-(1-7) at its natural receptors, Mas and MrgD, we tested whether C21 is also not AT2-specific but can stimulate the two Ang-(1-7) receptors, too.

Using cAMP as readout in receptor-transfected HEK293 cells, we generated pharmacological proof that Mas and MrgD are functional receptors for C21, whereby the three receptor blockers, A779, D-Pro⁷-Ang-(1-7), and PD123.319 showed receptor-specific effects towards C21 signalling. Furthermore, C21 elevated the cAMP concentration in primary cells such as mesangial cells. However, significant increase in cAMP levels, but not in PKA activity, was still detectable in mesangial cells isolated from AT2-deficient mice, but completely blunted in Mas/MrgD-double knockouts. In silico modelling was performed to illustrate the similarities and differences between C21, AVE0991, and Ang-(1-7). Our results identify C21 as not being a specific AT2 receptor agonist but also interacting with Mas and MrgD. Therefore, the partial overlap in beneficial effects of Ang-(1-7) and C21 might be based on the stimulation of the same receptors under specific pathophysiological circumstances. This also enforces the revisit of such publications which concluded on AT2 function by only using C21.
Quantification of perioperative ctDNA levels and inflammatory markers may identify patients at risk of early recurrence in colon cancer

CA Fleming¹,², DP O'Leary¹,², JH Wang¹,², HP Redmond¹,²

¹Surguvant Research Centre, Cork University Hospital, Cork, Ireland
²Department of Academic Surgery, Cork University Hospital, Cork, Ireland

Introduction: Peri-operative inflammation has been extensively highlighted in cancer patients as a potential therapeutic target. Circulating tumour DNA (ctDNA), detected in serum samples correlate with disease burden and may increase prior to radiological or macroscopic evidence of disease. We aimed to identify if identification of high levels of ctDNA and inflammatory markers in the peri-operative period may identify those at risk of early recurrence in colon cancer.

Methods: Non-metastatic colon cancer patients, aged 18-85 years, undergoing elective curative surgery were included. Exclusion criteria included: liver/renal disease; chronic inflammatory or immunodeficiency disorders; BMI>40; steroid use/immunosuppression therapy. Serum samples were taken at seven time points: pre-operatively; post-operatively at 3 hours, 6 hours, 24 hours, 48 hours, 72 hours and five days. IL-6, TNF-α, VEGF and IFN- were measured. ctDNA was extracted using the QIAamp Circulating Nucleic Acid kit (QIAGEN). Statistical Analysis was performed using IBM SPSS, v.22.

Results: Thirty five samples were analysed (from five patients), two with recurrence and three disease-free at 2-years. Mean age was 67 years (range 58-78. Patients without recurrence had Stage 2A, 3B and 3C disease at presentation. Recurrence patients had stage 2B and 3C disease at presentation. Peri-operative inflammation and ctDNA levels in recurrence patients were not influenced by post-operative complications. In recurrence patients, ctDNA and inflammatory markers all peaked on (post-operative day) POD5. Peak ctDNA and VEGF levels at POD5 have the strongest correlation with early recurrence (ctDNA, r=0.866, p=0.058; VEGF, r=0.884, p=0.047).

Conclusions: Perioperative ctDNA and inflammatory marker patterns may predict early recurrence oncological outcomes in colon cancer.
The impact of the fermented milk drink kefir on physiology, immunology and behaviour.

M van de Wouw¹,², AM Walsh¹,³,⁴, F Crispie¹,³, L van Leuven¹, M Boehme¹, PD Cotter¹,³, TG Dinan¹,⁵, JF Cryan¹,²,⁵

¹APC Microbiome Institute, Cork, Ireland
²Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
³Teagasc Food Research Centre, Fermoy, Ireland
⁴Microbiology Department, University College Cork, Cork, Ireland
⁵Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland

Mounting evidence suggests a role for the gut microbiota in modulating brain physiology and behaviour through the bi-directional axis called the microbiota-gut-brain axis. As such, the gut microbiota represents a potential therapeutic target for influencing the centrally-mediated events and behaviour including anxiety and depression. The fermented milk drink kefir has recently been shown to have anti-inflammatory properties, and to influence microbiota diversity and complexity. We sought to further investigate this by administrating two different kefirs or milk control for 3 weeks in male adult mice and assess anxiety- and depressive-like behaviour, as well as markers of systemic immunity. We found that both kefirs decreased anhedonic or depressive-like behaviour in the female urine sniffing test, and both reduced bodyweight, independent of food intake and type of body mass (i.e. lean, fat and liquid). Both kefirs also reduced circulating granulocyte levels, a marker of inflammation. However, one kefir selectively decreased anxiety/repetitive behaviour in the marble burying test and induced a trend towards decreased depressive-like behaviour in the forced swim test. The same kefir also increased anti-inflammatory T regulatory cell levels in mesenteric lymph nodes. These results show that the fermented milk drink kefir can reduce bodyweight, inflammation and decrease anxiety- and depressive-like behaviour. In addition, our results show that many of the effects of kefir are kefir-specific, highlighting the need for thorough kefir characterization.
Incidence of Subsequent Stroke in Patients Attending the Rapid Access TIA Clinic in Cork University Hospital

K O'Brien¹, S Cronin¹,²

¹School of Medicine, University College Cork, Cork, Ireland
²Department of Neurology, Cork University Hospital, Cork, Ireland

Background

Transient ischaemic attack (TIA) is a harbinger for the imminent development of stroke. The ABCD² score clinical tool predicts 7- and 90-day stroke risk in TIA patients. The OXVASC study showed that ABCD² 0-4 predicts 3% stroke recurrences within 7 days whereas ABCD² 5-7 predicts 12% strokes, felt to reflect cases with atrial fibrillation or symptomatic carotid stenosis.

A rapid access ambulatory OPD clinic for patients with recent (1-7 days) TIA and ABCD² below 4 is run in CUH.

Objectives

We sought to evaluate (1) recurrent 7-day and 90-day TIA/stroke risk; (2) rate of carotid endarterectomy and (3) rate of de novo anticoagulation among the first 250 low risk patients attending the rapid ambulatory TIA Clinic at Cork University Hospital.

Methods

Data was collected from the iSoft Clinical Manager software, city wide imaging platforms, chart review and by postal survey.

Results

Risk for recurrent TIA and stroke was 0% and 0.4% at 7d and 90d respectively. Among patients with confirmed TIA, 9.2% had carotid endarterectomy and 4.3% were anticoagulated. The postal survey had a 35.2% response rate and did not identify any additional recurrences.

Conclusion
It is safe to see patients with ABCD2 scores of 0-4 at the TIA clinic as these patients are at low risk of subsequent stroke following appropriate treatment/intervention. Despite low scores, 13.5% had a high risk aetiology (AF or symptomatic carotid stenosis) identified and treated.

P25

An Oxytocin Feast: Novel signalling of the Oxytocin Receptor with the Ghrelin Receptor and Glucagon like Peptide 1 Receptor in Social Eating

SE Wallace Fitzsimons1,3, B Chruścicka1, C Druelle1, TG Dinan1,2, JF Cryan1,3, H Schellekens1,3

1APC Microbiome Institute, University College Cork, Cork, Ireland
2Dept. of Psychiatry, University College Cork, Cork, Ireland
3Dept. of Anatomy and Neuroscience, University College Cork, Cork, Ireland

The Oxytocin receptor (OXTR) is suggested to play a central role in social behaviours, anxiety, depression and more recently in food preference and other eating behaviours. Similarly, the central ghrelin (GHSR1a) and glucagon like peptide 1 (GLP1r) receptors have been shown to be involved in appetite regulation and food intake. Previous dogma dictated that such GPCRs signal as monomeric proteins, but pharmacological and biochemical studies have demonstrated the existence of functional homo- and heterodimers. Central co-expression of the GHSR1a, GLP1r and OXTR receptors in areas such as the hypothalamus and hippocampus, led us to investigate the potential crosstalk and heterodimerisation between these receptors and its relevance to social eating.

Lentiviral plasmids encoding the OXTR–tagged red fluorescent protein were packaged into lentiviral vectors and transfected into stable HEK cell lines expressing GHSR1a or GLP1r receptor tagged with a green fluorescent protein. Similarly, plasmids for GLP1r or GHSR1a-RFP were transfected into HEK cells expressing OXTR-GFP. Using confocal microscopy, co-localisation and co-internalisation of receptors was analysed. Functional assays including calcium mobilisation assays, IP-1 assays and cAMP assays were used to evaluate any alterations in receptor signalling.

We demonstrated that the OXTR receptor interacts with the GHSR1a and GLP1r receptors, indicating they may function as possible heterodimers. Moreover, functionality was altered compared to their homodimer counterparts. Future work will investigate interactions ex vivo using proximity ligation assay in brain slices and functional interactions in hypothalamic primary cell cultures. Functional changes following GPCRs crosstalk may shed some light on the susceptibility of certain individuals to have changes in eating behaviour as a consequence of anxiety and stress or following social settings.
Synthetic Biology In The Driving Seat Of The Bioeconomy

Y Flores Bueso¹,²,³, M Tangney¹,²,³

¹Cork Cancer Research Centre, University College Cork, Cork, Ireland
²SynBioCentre, University College Cork, Cork, Ireland
³APC Microbiome Institute, University College Cork, Cork, Ireland

Synthetic Biology (SB) has evolved as an umbrella term, representing a methodological framework adopted by a variety of research streams aligned in the quest to create synthetic life and downstream products. Its unprecedented pace of growth is evidence of the support provided by governments, the efforts made in developing a thriving community, and programmes facilitating routes to market.

The SB community seeks to annul the primary pitfalls of traditional biotech in terms of cost, reliability and productivity by discontinuing ad hoc practices often characteristic of traditional biotechnology by implementing systematic methods. Also, it is perceived that the reduced skill set, community repositories etc. will lead to a different breed of idea generators than traditional biotech, thus leading to previously unthought-of products and markets. Further to that, the SB community from the outset, placed much attention on bioeconomy aspects (product development needs, routes to market etc.) in order to avoid commercial failures observed with biotech. As a consequence, the SB is revolutionising the biotech industry and its applications are poised to conquer previously unthought-of markets.

We discuss the importance of the SB industry in the bioeconomy, and how it was forged by two key factors; i) the SB approach to R&D distinguishing it from the traditional, and ii) the unique nature of the field’s carefully designed, all stakeholder inclusive, ‘community-directed evolution’.
A 3D cell culture model for candidate drug screening in Pancreatic Ductal Adenocarcinoma

JD Murphy\textsuperscript{1}, P Fernandes\textsuperscript{1}, JA Barry\textsuperscript{1,2}, KS Gill\textsuperscript{1}, DM Soden\textsuperscript{1}, PF Forde\textsuperscript{1}

\textsuperscript{1}Cork Cancer Research Centre, University College Cork, Cork, Ireland
\textsuperscript{2}Blood Cancer Network Ireland, (BCNI),

Cell culture has been in use in cancer research since the isolation of HeLa cells in 1951. Currently there are thousands of cell lines representing various cancer subtypes and genetic modifications. These are an invaluable tool in research but are mostly used in 2 dimensional models that do not adequately represent the tumour microenvironment. This can be overcome to some degree through the use of 3D cell culture, in which adherent cells are grown in a spheroid shape, introducing a layer of heterogeneity in access to drugs, oxygen and metabolites. This creates a varied response to candidate treatments and may better bridge the gap in the massive drop off between \textit{in vitro} and \textit{in vivo} drug development.

Our work focuses on combining physical therapies with various candidate modulators in order to treat pancreatic ductal adenocarcinoma (PDAC) which has the highest ratio of mortality to morbidity of any cancer subtype, the 5 year survival for this disease currently stands at less than 10\%. The focus of this research is to validate previous work by our group in which we analyse the cellular response to our combinational treatment and attempt to increase targeted tumour cell death.
Engagement of Fas differentially regulates the production of LPS-induced pro-inflammatory cytokines and type I Interferons

C Lyons\textsuperscript{1}, P Fernandes\textsuperscript{3}, K Brennan\textsuperscript{4}, SL Doyle\textsuperscript{4}, A Houston\textsuperscript{2}, E Brint\textsuperscript{1}

\textsuperscript{1}Pathology, UCC, Cork, Ireland
\textsuperscript{2}Medicine, UCC, Cork, Ireland
\textsuperscript{3}CCRC, UCC, Cork, Ireland
\textsuperscript{4}School of Medicine, TCD, Dublin, Ireland

Best known for its role in apoptosis, recent reports suggest that Fas (CD95) signalling is also involved in other cellular responses including inflammation. Whilst Fas and its adaptor protein FADD have been previously shown to negatively regulate LPS-induced pro-inflammatory responses, their role in LPS-induced type-I Interferon production is unknown. Here we demonstrate that Fas engagement on THP-1 macrophages using an agonistic Fas antibody CH11, augments LPS-induced NF-κB responses, causing an increase in the production of TNFα, IL-10, IL-8, IL-6 and IL-12. Conversely, co-stimulation with both LPS and CH11 causes a significant reduction in the level of IFNβ production. This differential effect involves the Fas adaptor FADD as, whilst LPS-induced IL-6 production was increased in FADD\textsuperscript{-/-} murine embryonic fibroblasts, LPS-induced IFNβ production was significantly reduced in these cells. Overexpression of a dominant negative form of FADD, the FADD-Death Domain (FADD-DD), in the RAW264.7 macrophage cell line, inhibits LPS-induced IFNβ-luciferase but not LPS-induced NF-κB luciferase. In contrast, overexpression of full-length FADD inhibited LPS-induced NF-κB-luciferase activation but was seen to augment LPS-induced IFNβ-luciferase. Moreover, the FADD-DD inhibits TLR-4-, TRIF- and TRAM-induced IFNβ-luciferase production, indicating that FADD may be interacting with the TLR-4 pathway at the level of these TLR4 adaptor proteins. In conclusion, these data identify FADD as a novel component of the MyD88-independent pathway leading from TLR4 to Type-I Interferon production and moreover demonstrate that both Fas and its adaptor FADD can differentially regulate the production of LPS-induced pro-inflammatory cytokines and type I Interferons.
Bacteria tumour targeting and in situ delivery of therapeutics

Y Flores Bueso\textsuperscript{1,2,3}, S Cronin\textsuperscript{2,4}, M Tangney\textsuperscript{1,2,3}

\textsuperscript{1}Cork Cancer Research Centre, University College Cork, Cork, Ireland
\textsuperscript{2}SynBio Centre, University College Cork, Cork, Ireland
\textsuperscript{3}APC Microbiome Institute, University College Cork, Cork, Ireland
\textsuperscript{4}School of Biochemistry, University College Cork, Cork, Ireland

The tumour environment offers a unique set of conditions favouring the selective growth of certain bacteria species. Several strategies exploiting them as therapeutic agents have been examined. As with all therapeutic strategies, the key to success lies in achieving a suitable balance between efficacy and safety.

\textit{In situ} production of therapeutics in tumours allows for bioaccumulation (higher-doses) with reduced off-target effects. Non-invasive bacteria (lacking the ability to enter host cells) offer a safer alternative to invasive (pathogenic) bacteria. However, these bacteria are incapable of directly depositing therapeutic agents within target tumour cells.

Cell penetrating peptides (CPPs), are short peptides enabling the introduction of cargo through the membrane of mammalian cells. The successful protein transduction of cancer cells has been validated \textit{in vitro} and \textit{in vivo} following administration of purified recombinant protein. We hypothesise that regulated \textit{in situ} bacterial production of CPPs-tagged proteins might facilitate selective intracellular delivery of proteins to tumour cells.

**Aim:** The aim of this study is to investigate the potential of intra-tumoural bacteria to express proteins capable of entering tumour cells.

**Preliminary Results:** The production and secretion of a CPP-GFP was demonstrated. The transduction of cancer cells \textit{in vitro} and \textit{in vivo} was demonstrated via FACS analysis.

These novel preliminary data indicate that bacteria can produce self-transducing proteins within tumours, suggesting a valid role for non-invasive bacteria in tumour therapeutic strategies.
Investigation of the role of IL-36 cytokines in colon cancer

C O'Donnell¹, K Baker², S Melgar⁴, P Walsh³, A Houston¹, E Brint²

¹Dept. Of Medicine, University College Cork, National University of Ireland, Cork, Ireland
²Dept. Of Pathology, University College Cork, National University of Ireland, Cork, Ireland
³Dept. Of Clinical Medicine, School of Medicine, Trinity College Dublin, Ireland
⁴APC Microbiome Institute, University College Cork, National University of Ireland, Cork, Ireland

The IL-36 cytokines are a recently described subset of the IL-1 family of cytokines, shown to play a role in the pathogenesis of intestinal diseases such as Inflammatory Bowel Disease (IBD). Given the link between IBD and colitis –associated cancer, as well as the involvement of other IL-1 family members in intestinal tumorigenesis, the aim of this work was to investigate whether IL-36 cytokines play a role in the pathogenesis of colon cancer. Expression of both IL-36α and IL-36γ, mRNA and protein, were found to be significantly increased in colorectal cancer tissue compared to adjacent non-tumour tissue whilst expression of both the IL-36R and IL-36RN was unchanged. IL-36b was not detected. Whilst no IL-36 cytokine appears to affect either cellular migration or invasion, IL-36g strongly increased cellular proliferation in two colon cancer cell lines. IL-36α and IL-36γ induced high levels of expression of pro-tumorigenic chemokines CXCL-1, CCL-2, CCL-20 and IL-8 in colon cancer cells. Taken together, these data show that certain IL-36 cytokines are increased in colon cancer and that tumour cells may respond to IL-36 ligand stimulation in terms of a positive increase in proliferation and an induction of pro-tumorigenic chemokines.
Assembling proteins with light

S Buckley1,2,4, Y Flores Bueso1,2,3, M Tangney1,2,3

1Cork Cancer Research Centre, University College Cork, Cork, Ireland
2SynBio Centre, University College Cork, Cork, Ireland
3APC Microbiome Institute, University College Cork, Cork, Ireland
4School of Biochemistry, University College Cork, Cork, Ireland

**Background:** Plants’ reaction to external light stimulus relies on phototropins. This reaction is triggered by a LOV (Light Oxygen Voltage) protein domain. The light activated function of LOV domains makes them an attractive inducible tool for use in biotechnology. iLID, a synthetic LOV domain variant, holds an ssrA degradation tag that will bind to a SspB adaptor when exposed to blue light.

Previous work has shown that fluorescent proteins can be genetically split, and reassembled to a functional dimer at the protein level. Fluorescence is a convenient readout for dimerization of split protein fragments. This could be performed transiently, upon the exposure to blue light, with a LOV domain. Here, we hypothesise that split fluorescent proteins can be reassembled transiently using an iLID-SspB system.

**Aim:** The aim of this project is to reconstitute split fluorescent proteins and induce protein-protein interaction (PPI) of two synthetic proteins, transiently, with light.

**Results:** The correct design and expression of 13 devices in *E. coli* was validated by *in silico* protein modelling, sequencing, PAGE and Western blots. Fluorescence analyses demonstrated the interaction of synthetic split proteins under the influence of blue light.

**Conclusion:** A novel method for inducing the reconstitution of split fluorescent protein fragments was designed and examined. This study indicates the potential for controllable synthetic protein interaction systems for exploitation in multiple biotechnology fields, such as diagnostics, and as research tools.
A Smoke-Free UCC Campus in sight?

N Skrabanek, Z Kabir

Epidemiology & Public Health, University College Cork, Cork, Ireland

Introduction

The aim of this study was two-fold: to ascertain smoking prevalence and tobacco use among students and staffs of University College Cork (UCC); to determine their knowledge, attitudes, practices and perceptions of both outdoor environmental-tobacco-smoke and a smoke-free campus policy.

Methodology

This is a cross-sectional online Survey-Monkey study through an anonymous web-based questionnaire sent out to by e-mails to approximately 18,000 students and 2800 staffs of UCC before the summer break in 2017. Both descriptive and inferential statistics were performed.

Results

1,015 eligible survey responses were analysed. Overall, smoking prevalence was 24.4%. Use of e-cigarettes and other tobacco products was low. 56.5% of respondents were exposed to secondhand smoke (SHS) at least a few times a week; 72.3% considered SHS harmful, while 27.7% thought vapour from e-cigarettes was harmful. Marked differences were noted between smokers and non-smokers: 47.7% of smokers believed outdoor SHS was harmful, whereas 85.6% of never smokers believed the same. A greater proportion of respondents were unsure about the harmful effects of e-cigarettes (36.7%) as compared to that of cigarettes (10.2%). 59.5% believed that further smoking restrictions should be introduced on campus. The most popular forms of bans were designated smoking areas (46.3 %) and smoke-free zones (64.0 %) around entrances; 21.5% supported a 100% smoke free campus. The most popular forms of enforcement were fines (41.6%) and verbal warnings (30.0%).

Conclusion
Despite support for some form of smoking restrictions on University campus, a 100% smoke free UCC campus was not totally supported by the current evidence.

P33

Combination of electroporation delivered metabolic modulators with low-dose chemotherapy and the immune response in Osteosarcoma

KS Gill, P Fernandes, DM Soden, PF Forde

Cork Cancer Research Centre, University College Cork, Cork, Ireland

Osteosarcoma is the most common (75%) high-grade malignant tumour of the skeletal system in patients aged between 10-25 years, with an annual incidence of one thousand new cases diagnosed in the United States, of which about 450 of these are in children and teens.

The high mortality rates in osteosarcoma are largely a result of both intrinsic and acquired resistance (60%) to currently used polychemotherapies that lead to multidrug resistant phenotypes and the occurrence of ‘second malignancies’. Neoadjuvant chemotherapy has not been shown to improve long-term prognosis of patients compared to adjuvant chemotherapy alone.

Therapy efficacy and survival outcome could potentially be increased by methods of subverting therapy resistance and re-establishing sensitivity of osteosarcoma to existing treatments. While tremendous progress has been made in the treatment of osteosarcoma, there is a critical need for the development of novel therapies to improve patient survival.

Electroporation is a non-thermal, cell permeabilising technology that renders the treated cell membranes permeable to poorly permeant anti-cancer drugs thus facilitating a potent local cytotoxic effect from the improved cell membrane porosity. Electrochemotherapy combines electroporation and local or systemically administered chemotherapeutic agents.

Metabolic modulators in combination with chemotherapy has been shown to be effective in cancer treatment, due to increase sensitivity of cancer cells from depletion of intracellular ATP levels from the glycolytic modulation.

The aims of this study were to examine the cytotoxic effects of electroporation delivered metabolic modulators and low-dose chemotherapy in Osteosarcoma models and to determine the anti-tumour immune response associated with the treatment.
Stemness induced by Electrochemotherapy in Pancreatic Adenocarcinoma

M Shahzad Ali\textsuperscript{1,2}, KS Gill\textsuperscript{1}, D Cilloni\textsuperscript{2}, G Saglio\textsuperscript{2}, PF Forde\textsuperscript{1}

\textsuperscript{1}Cork Cancer Research Centre, University College Cork, Cork, Ireland
\textsuperscript{2}Department of Clinical and Biological Sciences, University of Turin, Turin, Italy

Among the reasons for cancer recurrence, preexisting cancer stem cells (CSCs) or tumor initiating cells are considered the most likely cause due to their properties of self-renewal, pluripotency, plasticity and tumorigenicity. It has been demonstrated that preexisting cancer stem cells derive from normal stem cells and differentiated somatic cells that undergo transformation and dedifferentiation respectively under certain conditions. Recent data has been provided to support the existence of CSCs in human blood cell-derived cancers and solid organ tumors of the breast, brain, prostate, colon, and skin, and it has been suggested the CSC population as a source of chemotherapy and radiation-therapy resistance within tumors. Here we assess the effect of the physical therapy such as electroporation/electrochemotherapy on stemness of cancer cells and how modulation of these observation have on electrochemotherapy.
The increasing use of gabapentinoids in intentional drug overdose: findings from the National Self-Harm Registry Ireland, 2007-2015

CD Daly¹, EG Griffin¹, DA Ashcroft², RW Webb², IP Perry¹,³, EA Arensman¹,³

¹National Suicide Research Foundation, University College Cork, Cork, Ireland
²Manchester Academic Health Sciences Centre, University of Manchester, Manchester, England
³School of Public Health, University College Cork, Cork, Ireland

Introduction: Intentional Drug Overdose (IDO) is a significant public health problem. There are growing concerns internationally regarding the misuse of pregabalin and gabapentin, drugs primarily intended to treat epilepsy, including their consumption in IDO. This research describes the trends in the prevalence of gabapentinoids involved in IDO, the profile of persons taking them and the associated drug overdose characteristics.

Methods: Data were obtained on presentations to emergency departments involving IDO recorded by the National Self-Harm Registry, Ireland (NSHRI) between January 1st 2007 and December 31st 2015.

Results: Presentations involving a gabapentinoid increased proportionally from 0.5% (n=40) in 2007 to 5.5% in 2015 (n=369). The majority of IDOs involving a gabapentinoid were made by females (59.9%), with over one third (37.2%) involving alcohol. Compared to IDOs involving other drugs, presentations with a gabapentinoid were made by older persons (32 vs 37 years). Presentations with a gabapentinoid involved a significantly greater median quantity of total tablets in IDO (30 vs 21, p=<0.001), with over a quarter (27.4%) of such presentations involving the ingestion of 50 tablets or more per act. Admission to hospital was significantly more common following IDOs with a gabapentinoid, compared to those without (49% vs 41%, p=<0.001).

Conclusion: This research describes the increasing use of gabapentinoids in IDO and reveals the profile and overdose and next care characteristics of such presentations. These findings inform prescribers of populations at risk of IDO with gabapentinoids and underlines the importance of routine monitoring for signs of misuse of these drugs in patients.
Factors associated with walking in older medical inpatients

R McCullagh¹, D Dahly², NF Horgan³, S Timmons¹

¹Centre for Gerontology and Rehabilitation, School of Medicine, UCC@ St Finbarr’s Hospital, Cork, Ireland
²Department of Epidemiology and Public Health/ Clinical Research Facility, School of Medicine, UCC, Cork, Ireland
³School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland

Aim: To identify patient characteristics and daily events that could influence walking among older medical inpatients.

Methods: Medical inpatients aged ≥65 years, premorbidly mobile, with an anticipated hospital stay ≥3 days, were recruited. Walking (Stepwatch Activity Monitor) and potential influencers of walking were recorded for 7 days or until discharge, including medical status, assigned bed-rest, walking aids or assistance, tethering treatments (catheters/intravenous lines etc.), agitation/confusion, fatigue, pain, and fear of falling. Linear mixed effects models were used to measure the associations between (log) step-count and potential influencers, and patient characteristics on admission: age, sex, height, weight, physical performance (SPPB), medications, and illness severity (CIRS-G).

Results: Data from 147 patients were analysed. In the adjusted mixed effects model, walking increased linearly (12%, 95% CI 2% - 23%) for each day. However, the mixed effects model (with patient-level random intercept and slope factors) fit the data best, suggesting considerable patient-level variability in step-count exists. Patients walked most on Wednesdays (1.26 CI 1.04, 1.53) and least on the first observed day (0.51 CI, 0.42, 0.62). More walking was associated with better physical performance on admission (1.15, CI, 1.08, 1.22), and with patients’ improving medical status (1.33 CI 1.07-1.64). Less walking was associated with tethering treatments (0.71, CI 0.56, 0.91) and instructed bed-rest (0.31, CI 0.21, 0.45).

Conclusion: Both between- and within-patient walking was variable, even when adjusted for patient characteristics on admission. Tethering treatments may possibly be a modifiable barrier. Physical performance on admission may be a useful indicator of walking.
Dynamic Gastrointestinal Serotonergic Responses to an Acute Stressor: Role of Host Genetics

JM Lyte¹, MS Goodson², N Kelley-Loughnane², TG Dinan¹,³, JF Cryan¹,⁴, G Clarke¹,³

¹APC Microbiome Institute, University College Cork, Cork, Ireland
²711th Human Performance Wing, Air Force Research Laboratory, Dayton, USA
³Psychiatry and Neurobehavioral Science, University College Cork, Cork, Ireland
⁴Anatomy and Neuroscience, University College Cork, Cork, Ireland

Objective: Host genetics influence acute stress response which may alter gastrointestinal function. Gut-derived serotonin (5-HT) exerts physiologically and clinically important local and systemic effects. The role of host genetics on gastrointestinal serotonergic response to acute stress is poorly understood. We sought to define the gastrointestinal serotonergic response to and recovery from acute stress in genetically-distinct mice strains.

Methods: Adult male NIH Swiss-Webster, BALB/c, and C57/BL6 mice were randomly allocated to the unstressed control or stress group. Stressed animals were subjected to 15min restraint stress (n=4-8 mice/timepoint/strain) and sacrificed post-stressor +0, 5, 15, 30, 45, 60, or 240min. Plasma corticosterone (CORT), a canonical measure of hypothalamic-pituitary-adrenal-(HPA)-axis activation, was assayed using ELISA. Colonic and ileal 5-HT and 5-HIAA were measured via HPLC. Results were analyzed by student’s t-test or ANOVA, where applicable, and statistical significance was set at p<0.05.

Results: CORT was elevated (p<0.05) after restraint stress compared to control in each strain. C57/BL6 exhibited greater (p<0.05) CORT post-stressor compared to BALB/c or NIH Swiss-Webster. Colonic 5-HT was higher than ileal in all mouse strains. Intestinal 5-HT and 5-HIAA were elevated (p<0.05) post-stress in C57/BL6 compared to other strains.

Conclusions: Confirming that host genetics influence stress response, the C57/BL6 strain displayed the largest HPA-axis post-stress activity. C57/BL6 also had higher colonic and ileal 5-HT post-stressor. Further studies are required to understand the implications of these findings for the control of stress-induced 5-HT-mediated gastrointestinal symptoms.
and to assess how the gastrointestinal microbiota and microbial metabolites might regulate gastrointestinal serotonergic response to acute stressors.

P41

The virtually mature BNP (BNP1-32) is a precursor for the more potent BNP1-30

A Schwiebs¹, A Moore², Y Wang¹, X Zhu³, K Pankow⁴, WE Siems⁴, T Walther²

¹Department of Cardiology, Justus-Liebig-Universitat, Giessen, Germany
²Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland
³Centre for Cardiovascular and Metabolic Research, University of Hull, Hull, United Kingdom
⁴Leibniz-Institut fur Pharmakologie, Berlin, Germany

The mature B-type natriuretic peptide (BNP1-32) exerts vasorelaxing and cardioprotective activity. BNP is used as a biomarker for the diagnosis of cardiopathological conditions and as a drug for the treatment of such. BNP1-32 has a short half-life time and, like angiotensin II, bradykinin, and other vasoactive peptides, can be enzymatically truncated forming bioactive metabolites. We aimed to investigate the metabolism of BNP1-32 in lung, to identify potential new BNP metabolites, and to disclose their biological activity compared to mature BNP1-32, in vitro and in vivo.

Using LCMS, we identified a new BNP metabolite, BNP1-30, being generated in the lung by endothelin-converting enzyme-1. BNP1-30 is more efficient in stimulating the natriuretic peptide receptor (NPR) A and, in contrast to BNP1-32, is also able to stimulate the NPRB. In vivo, BNP1-30 reduced the mean arterial blood pressure of normotensive mice after acute infusion significantly more than BNP1-32. In a model of severe hypertension, a 3-day infusion of BNP1-30 was able to reduce systolic blood pressure by 30 mmHg and to improve markers of heart failure, while BNP1-32 was without significant effect. Importantly, BNP1-30 could not only be detected in rodents but is also generated in the human lung.

Our results suggest that BNP1-32 is only the precursor for the biologically more active BNP1-30, leading to a fundamental extension of the natriuretic-peptide system. Due to the expanded activity, BNP1-30 might be a promising treatment option for cardiovascular diseases. Furthermore, its potency as a new diagnostic marker of specific cardiac diseases should be evaluated.
Degradation of Ang-(1-7) in Different Mouse Organs

A Moore, I Ibifubara, T Walther

Department of Pharmacology and Therapeutics, School of Medicine and School of Pharmacy, University College Cork, Cork, Ireland

Angiotensin(Ang)-(1-7) has cardioprotective effects that serve to counter-regulate adverse effects of Ang II in the cardiovascular system. Ang-(1-7) inhibits the proliferative, cell growth promoting, and pressor effects of Ang II. Furthermore, it shows anti-fibrotic and anti-hypertrophic properties in preclinical models of myocardial infarction.

It is well accepted that Ang-(1-7) is primarily degraded to Ang-(1-5) by ACE in the cardiovascular system. However, we have preliminary results showing variations exist in Ang-(1-7) degradation pathways in various mouse organs. It is the aim of this study to quantify the metabolites in individual organs and to generate an organ-specific fingerprint of Ang-(1-7) truncation.

Our results show that after 10 minutes, Ang-(1-7) is degraded fastest in lung (1% of peptide remaining) and slowest in brain (86% of peptide remaining). Unsurprisingly, Ang-(1-5) was a major degradation product for organs with substantial ACE2 expression, such as lung and kidney. However, we identified Ang-(1-4) as another major degradation product in lung and kidney. In contrast, the major degradation product of Ang-(1-7) in the brain, ventricle, testis, and liver was Ang-(2-7). Ang-(1-7) was not at all converted in atrium membranes.

Ang-(1-7) degradation varies greatly in both speed and metabolites generated between mouse organs. The necessity to update the relatively old canonical Ang-(1-7) degradation pathway is paramount for drug design and efficacy. By identifying and subsequently inhibiting the peptidases ultimately responsible for the metabolism/catabolism of Ang-(1-7), its circulating concentration can be increased, thus improving the benefits of the heptapeptide’s cardiovascular protective effects.
Evidence for Microcompartment-Mediated Metabolism in Urinary Tract Infection

K Dadswell\textsuperscript{1,2}, S Creagh\textsuperscript{4}, E McCullagh\textsuperscript{4}, J MacSharry\textsuperscript{2,3}, MB Prentice\textsuperscript{1,4}

\textsuperscript{1}School of Microbiology, University College Cork, Cork, Ireland
\textsuperscript{2}APC Microbiome Institute, University College Cork, Cork, Ireland
\textsuperscript{3}School of Medicine, University College Cork, Cork, Ireland
\textsuperscript{4}Department of Microbiology, Cork University Hospital, Cork, Ireland

Background: Urinary Tract Infections (UTIs) are common infections resulting from bladder access of gut bacteria. Uropathogenic E. coli (UPEC) gut commensals cause most UTIs. Central metabolism and catabolic pathways are essential for E. coli gut colonisation. Bacterial microcompartment-mediated metabolism of small carbon compounds promotes overgrowth of Enterobacterial pathogens. Eut microcompartment operons (utilisation of cell membrane-component ethanolamine) may function in UTIs.

Methods: 70 infected urine samples cultured, qRT-PCR for eut Operon expression. MALDI-TOF speciation, genome sequencing of isolates. HPLC for ethanolamine.

Results: E. coli eut operon mRNA transcription (eut R, eut BC) in 13% of urines. E. coli was the most prevalent isolate. Sequencing of 37 E. coli isolates assigned over 75% to Phylogroups B2 and D, representative of reported extraintestinal pathogenic E. coli. All strains contained complete eut operons. Twenty E. coli isolates (54%) contained a full dsdCXA (D-serine tolerance) operon associated with UPEC survival in host urine. Ten strains contained the intestinal (IPEC) marker astA gene encoding the EAEC heat stable toxin EAST1, atypical for UPEC. In vitro growth experiments confirmed E. coli isolates utilized ethanolamine in minimal media and artificial urine with growth enhancement and production of ethanolamine breakdown product. Microscopy showed close bacteria-host cell membranes association in urine.

Conclusions: Expression of the E. coli eut operon in infected urine was confirmed. Cell membrane-association of bacteria and in vitro growth advantage with ethanolamine suggests microcompartment-mediated metabolism offers a competitive growth advantage in infected uri
P45

Pilot project on electronic photo-triage of referrals for infantile haemangiomas

A Flynn, M Murphy

Dermatology, South Infirmary Victoria University Hospital, Cork, Ireland

Background:

The discovery of propranolol as an effective treatment for infantile haemangiomas (IH) has been one of the highlights of paediatric dermatology. Infants with high-risk IH treated earlier have more favourable outcomes. In an era of prolonged waiting lists and pressure on resources, consultant dermatologists need to have a triage system in place to determine what is high-risk, in order to optimise timing of consultation.

Aim:

The aim of this project was to identify high-risk IH by allowing general practitioners to send a photograph of the haemangioma via Healthmail to a paediatric dermatologist. The photographs were reviewed within five working days and the general practitioner was contacted with an outcome.

Results:

The project initiated November 2016. To date there have been 88 referrals. Eight of the referrals did not have a photograph attached. At photo-triage 84% (67/80) were infantile haemangioma, 10% (8/80) port-wine stain, 1% (1/80) vascular malformation and 5% (4/80) could not have a definitive diagnosis made. Age varied from less than 1 week to 57 weeks, with a mean age of 16 weeks. 31% were located on the face, 28% on the trunk, 19% limbs, 11% scalp, 5% ear, 4% genital and 2% on the neck. 46% (31/67) of the IH did not require treatment, 36% (24/67) had a routine review and 18% (12/67) required urgent review.

Conclusion:

This novel photo-triage study has been effective at identifying high-risk infantile haemangiomas for urgent review. Patients with low-risk IH and port-wine stains were
triaged appropriately, obliterating the need for urgent clinical review and saving resources.

P46

An exploration of the effectiveness of an educational intervention on the use of personal protective equipment in orthopaedic theatres

CD Duggan¹, CT Taylor¹,²,³

¹School of Medicine, University College Cork, Cork, Ireland  
²Department of Orthopaedics, Cork University Hospital, Cork, Ireland  
³Department of Orthopaedics, South Infirmary Victoria University Hospital, Cork, Ireland

Introduction: Personal protective equipment (PPE) is an important tool in medicine. It helps to protect staff from harm in the form of infection and injury. Protocols exist in orthopaedic surgery for the use of PPE but are not always adhered to. The use of PPE can significantly reduce staffs’ exposure to harmful radiation and infection.

Aim: To observe the compliance with PPE followed by an educational intervention and then further observations to assess the efficacy of the intervention.

Methods: Questionnaires were distributed to orthopaedic surgeons and theatre nurses (subjects) and used to guide the educational intervention. 40 orthopaedic cases requiring fluoroscopic guidance were observed noting: count of available PPE, the use of lead aprons, thyroid guards, eye protection, radioprotective eyewear, radioprotective gloves and other details of each procedure. The intervention, a PowerPoint presentation was presented to four different groups to ensure that as many subjects as possible were given the intervention.

A further 40 cases were observed post-intervention.

Results: Initial analyses indicated a significant (P < 0.05) increase in the use of thyroid guards by surgeons; 13/115 (11.3%) pre-intervention compared to 54/117 (46.1%) post-intervention. Pre-intervention, across all groups 95.7% (335/350) wore lead aprons and 32.1% (111/346) wore thyroid guards compared with 96.3% (341/354) and 46.2% (163/353) respectively post-intervention.

Conclusion: Initial analyses indicate that the educational intervention is effective in increasing compliance with thyroid guards by orthopaedic surgeons.
Real-time Monitoring of Biological Airborne Particles in the Hospital Environment

MF Fennelly\textsuperscript{1,2}, PF Feeney\textsuperscript{1}, DO'C O'Connor\textsuperscript{3}, NM Murphy\textsuperscript{4}, CC Casey\textsuperscript{5}, BP Plant\textsuperscript{4}, JS Sodeau\textsuperscript{1}, MP Prentice\textsuperscript{2,6}

\textsuperscript{1}Environmental Research Institute, University College Cork, Cork, Ireland
\textsuperscript{2}Department of Microbiology, University College Cork, Cork, Ireland
\textsuperscript{3}School of Chemical and Pharmaceutical Sciences, Dublin Institute of Technology, Cork, Ireland
\textsuperscript{4}Adult Cystic Fibrosis Center, Cork University Hospital, Cork, Ireland
\textsuperscript{5}College of Medicine and Health, University College Cork, Cork, Ireland
\textsuperscript{6}APC Microbiome, University College Cork, Cork, Ireland

Direct bioaerosol sampling is in limited use as a quality control measure in hospitals. However, research has shown that the approach can be used to monitor and control airborne microorganism spread, guide epidemiological investigation of nosocomial infectious diseases, and monitor biohazardous procedures. A major limitation of current (off-line) sampling methods for bioaerosols in hospitals is the requirement for conventional culture, which takes some time for analysis. UV excitation of molecules, such as amino acids and NAD(P)H, now offers the opportunity for real-time specific counting and characterisation of living cells in air by on-line detection of their intrinsic fluorescence.

The aim of project ReM-BAPHE is to assess two novel bioaerosol sensors termed Waveband Integrated Bioaerosol Sensor (WIBS-4A and WIBS-4+) as real time monitors for the detection of airborne biological particles in hospitals.

The results presented here demonstrate a proof of principle application for the light induced fluorescence monitoring technique in a severe respiratory illness ward at Cork University Hospital. The ward was chosen because the patients’ illnesses are directly affected by air quality. Hence, it is specially fitted with an air filtering system, which utilises a “DBD plasma” to ensure total destruction of viruses, bacteria, and moulds at a DNA level. Data are presented from a 7-day campaign held in January 2017. Trends in fluorescent particles concentration, shape and size over the campaign will be discussed but do provide clear evidence for increases in fungal/bacterial spore counts at visiting times and other periods of walk-in activity to the ward.
Superior capsular reconstruction for treatment of irreparable rotator cuff tears: early clinical results

DBL Garcia¹, RA Delaney², RE Kingston³

¹School of Medicine, University College Cork, Cork, Ireland
²Sports Surgery Clinic, Dublin, Ireland
³Bons Secours Hospital, Tralee, Ireland

Aim: Assess outcomes of irreparable rotator cuff tears treated with superior capsular reconstruction (SCR) using a porcine dermal xenograft.

Background: Pain relief and functional improvement vary with current non-arthroplasty techniques for massive, irreparable rotator cuff tears. Reverse shoulder arthroplasty may be more reliable, but high complication rates in younger patients and in revision reverse arthroplasty are cause for concern. Superior capsular reconstruction recreates superior stability, therefore improving overall function of the shoulder joint by restoring the glenohumeral fulcrum.

Methods: Pre-operative and post-operative shoulder range of motion, American Shoulder and Elbow Surgeons (ASES) score, subjective shoulder value (SSV), and visual analogue score (VAS) for pain were measured. Data were collected retrospectively from electronic medical records on 20 SCRs performed by two surgeons between July 2015 and November 2016. Post-operative reviews occurred at 12 weeks, 24 weeks, 12 months, 18 months.

Results: Fifteen males and five females, mean age 66.47 years, underwent SCR. Mean follow up 7.4 months, range 3 – 18 months. Eight patients were pseudoparalytic pre-operatively; in six of these patients the pseudoparalysis was reversed after SCR, one patient was still pseudoparalytic at 12 weeks, and one 66-year-old patient remained pseudoparalytic at 24 weeks. Overall, mean VAS improved from 7.44 pre-operatively to 1.72 post-operatively, p<0.0001. Mean ASES Score pre-operatively was 32.57 and post-operatively 78.00, p<0.0001. SSV improved from 32.5% on average pre-operatively to 70.0% post-operatively, p=0.001.
Conclusion: SCR can alleviate severe pain and disability from irreparable rotator cuff tears, significantly improving shoulder function. In patients unsuitable for reverse shoulder arthroplasty, SCR is a promising alternative.

P49

Missed opportunities for melanoma detection in secondary care

C Quinlan¹, S McCracken², E Tierney¹, C Heffron³, J Fitzgibbon³, C Murphy⁴, JF Bourke¹, M Murphy¹,²

¹Department of Dermatology, South Infirmary Victoria University Hospital, Cork
²School of Medicine, University College Cork
³Department of Histopathology, Cork University Hospital, Cork
⁴Department of Medical Oncology, Bon Secours Hospital, Cork

Introduction: Early detection of melanoma is associated with improved survival. The role of secondary care providers in early detection of melanoma has been rarely explored.

Aim: To identify inpatient and outpatient episodes in patients with intermediate and thick melanomas in the 5 years and 1 year prior to their diagnosis.

Methods: A multicentre, retrospective case review was conducted at five hospitals in the Cork/Kerry region. Databases at the five hospitals were reviewed. All patients with primary cutaneous melanomas of greater than or equal to 1mm Breslow depth from January 2013 to December 2014 were included. Data from the patient record enquiry for the 5 years prior to diagnosis was collected for each patient at each clinical site.

Results: 106 patients were included. The median Breslow depth was 2.3mm. 32 (30%) of the melanomas were located on the head/neck region. 67% had a secondary care interaction in the 5 years prior to their melanoma diagnosis and 42.5% in the year prior to diagnosis. Most of these hospital encounters were in the outpatient clinic (57.5%), but almost one third (31%) had an inpatient admission in the five years prior to diagnosis and 10% in the year prior to diagnosis.

Discussion: A significant opportunity exists to improve early detection of melanoma in secondary care. Patients with intermediate and thick melanomas are being seen in secondary care facilities in the years prior to their diagnosis. Education campaigns directed at secondary care providers should be implemented to encourage them to perform skin assessment as part of clinical examination.
International research consistently shows evidence for an association between sensationalised media reporting and suicidal behaviour. This study examined the quality of media reporting of suicide in Ireland and adherence to media guidelines.

In accordance with the criteria outlined in the media guidelines for reporting suicide, 243 media articles were screened and analysed for quality of reporting of four high profile cases of suicide that occurred between September 2009 and December 2012.

A minority of articles contained sensationalised language (11.8%), placed reports on the front page of the newspaper (9.5%), published inappropriate photographs (4.2%) or mentioned location of suicide (2.4%), in compliance with the media guidelines. However, in the majority of articles analysed, journalists did not refer to appropriate support services for people vulnerable to, and at risk of suicide (75.8) or mention wider issues (53.8%). Overemphasis of community grief (48.3%) was also common. Nearly all articles (99.2%) breached at least one guideline and 58.9% of articles were found to breach three or more guidelines.

The quality of media reporting of suicide in Ireland is of a sufficient standard in certain key areas, however, important challenges remain. Increased monitoring by media monitoring agencies, regulators and government departments is required, particularly with the emergence of social media and the internet. Guidelines need to be positively reinforced and implemented on an on-going basis. Implementation should be conducted using a pro-active approach and form part of the curriculum of journalists and editors. The inclusion of guidelines for reporting suicide in press codes of conduct also warrants consideration.
Attitudes towards an Augmented Exercise Programme in Elderly inpatients in MUH

MP McInerney\textsuperscript{1}, M McCarthy\textsuperscript{1}, R McCullagh\textsuperscript{2}, S Fox\textsuperscript{2}, S Timmons\textsuperscript{1, 2}

\textsuperscript{1}School of Medicine, University College Cork, Cork, Ireland  
\textsuperscript{2}Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork, Cork, Ireland

**Background:** Older patients often experience functional decline in hospital due to factors including immobilisation and deconditioning. In the Mercy University Hospital (MUH) a randomised, controlled clinical trial assessed the effect of an Augmented Prescribed Exercise Programme (AEP) on the outcomes of frail elderly inpatients. A qualitative assessment of such interventions is important to understand how older people perceive the intervention, and to inform how they should be delivered for maximum effect.

**Aim:** To explore the attitudes towards, and perception of, exercise in frail elderly inpatients taking part in an AEP.

**Design:** This was a qualitative study; semi-structured interviews were conducted, transcribed and analysed using thematic analysis.

**Settings/participants:** In total, 13 people participated, including patients in the active arm (n=9) and the sham arm (n=4) of the AEP in MUH.

**Results:** Most participants (n=9) correctly identified what arm of the trial they were on. 7/9 in the Intervention arm and 2/4 in the Sham arm. Participants’ perception of what active exercise is, was largely based on their previous baseline of activity, and walking was used as a measure of activity. Participants stated ‘maintaining independence and mobility’ as motivation to participate. Frailty, mobility, fear of falling were identified as barriers to exercising in general. Improving mobility, and reducing frailty were also identified as motivating factors to participate.
Conclusions: Perception of exercise varies depending on their previous levels of mobility and exercise. While generally positive towards an APEP, a lack of intrinsic motivation and a combination of other barriers can prevent full participation in such programmes.

P52

Limitations of Neuroanatomy Web-resources

MAJ Javaid, HS Harriet Schellekens, JC John Cryan, AT Andre Toulouse

Anatomy and Neuroscience, University College Cork, Cork, Republic of Ireland

Neuroanatomy is a difficult topic and online resources can facilitate learning intricate neuroanatomical concepts. We have sought students’ perception regarding limitations of existing resources in context of learning neuroanatomical pathways. Deciphering such limitations will have clinical implications because impaired understanding of neuroanatomy of medical students and doctors has been linked with their lack of confidence to manage neurological patients (NEUROPHOBIA).

An exhaustive search for neuroanatomy web-resources was done using custom search strings. Filtration through inclusion/exclusion criteria generated 159 web-resources. Those containing 1) only histology-related information, 2) being non-interactive and 3) non-comprehensive, were excluded, leaving an inventory of 24 resources. This was narrowed down to 13 and subjected to ‘educators-evaluation criteria’. Five anatomy educators ranked these based on their usefulness in context of student-learning of spinal pathways. The top three existing web-resources, were subsequently compared against each other by 42 undergraduate UCC students (medical, 3rd-year neuroscience).

Educators’ evaluation revealed that web-resources were overall limited in conforming to educational and cognitive learning standards. Students perceived that following pedagogical domains were best employed, in the top-ranked resource compared to other resources, in terms of their usefulness in aiding neuroanatomy-learning: 1) clarity of explanation, 2) explanation of key principles, 3) step-by-step drawing of pathways, 4) usage of cross-sectional images, 5) quizzes, 6) radiology-images, 7) animations, 8) 3D computer models and 9) solving neurological cases and 10) features helping in 3D visualization of brain structures.

Students’ preferences will help infer reasons underlying usefulness of various web-learning features. This will inform instructional design of future resources to better
achieve learning outcomes for undergraduate students and reduce the prevailing neurophobia.
personalised health and social care services that serve to enhance care relationships rather than diminish them.

P55

The impact of breast feeding on stress, cognition and the gut microbiota in adults.

AM Cusack¹, PJ Kennedy¹, D Mullins³, C Stanton², JF Cryan¹, P O'Toole³, TG Dinan¹

¹Laboratory of NeuroGastroenterology, Alimentary Pharmabiotic Centre, University College Cork, Cork, Ireland
²Food Research Centre, Teagasc, Moorepark, Fermoy, Cork, Ireland
³Department of Microbiology, University College Cork, Cork, Ireland

Humans live in a symbiotic relationship with the gut microbes providing them with a constant source of nutrition, while in return they help us in a variety of ways including enabling optimal brain development and subsequent functioning. At birth the human brain is highly underdeveloped and the gut is largely sterile. Initial colonization of the gut microbiota during the postnatal stages of central nervous system and brain development plays a key role in later hypothalamic pituitary adrenal axis and immune response to stress, behaviour and cognition. A major source of bacterial colonization of the infant gut is through the bacteria from breast milk, which has been reported to contain more than 700 species. In this study 30 breast fed males and 30 formula fed males aged 18-24 years were recruited. Neuroendocrine responses to stress were determined by collecting multiple saliva samples for cortisol analysis during the Tier Social Stress Test (TSST) and to measure the cortisol awakening response (CAR). Stool samples were collected to establish the composition of the gut microbiota. The participants completed self-reporting questionnaires to assess stress, depression and anxiety. The Cambridge Neuropsychological Test Automated Battery (CANTAB) was used to assess cognition. Studies on the gut microbiota may play an important role in advancing the understanding of their role in cognition and stress.
Aim: A review of the literature paints a strong picture of inflammatory dermatological and rheumatological conditions having negative effects on oral health and oral-health related quality of life. The purpose of this case controlled study is to assess the Oral Health status of Dermatological and Rheumatological patients with a chronic inflammatory diagnoses requiring systemic therapy. The hypothesis is that these patients have more oral symptoms impairing their oral health than healthy controls.

Methods: An oral health assessment will be performed on 100 patients (50 cases and 50 controls) randomly selected from dermatology and rheumatology outpatient clinics in CUH and SIVUH. The oral health assessment comprises of an Oral Health Questionnaire and an Oral Health Exam using internationally standardised and validated templates from the World Health Organisation (WHO). The 50 patient cases will have physician diagnosed inflammatory dermatological or rheumatological diagnoses requiring systemic therapy and 50 patient controls will have no inflammatory dermatological or rheumatological diagnoses requiring systemic therapy.

Results: Data collection will not be completed until the middle of October due to the fact that a number of the clinics necessary for this project are only held once a month.

Conclusion: Aim to show an association between poorer oral health and oral health related quality of life in patients with inflammatory dermatological and rheumatological conditions requiring systemic therapy.
Incidence, associations, and impact of antibodies of undetermined significance in solid-phase technology.

M Bourque, R Barty, Y Liu, G Wang, N Ramsay, R Movilla, A Elahie, A Iorio, N Heddle, MP Zeller

1School of Medicine, University College Cork, Cork, Ireland
2McMaster Centre for Transfusion Research, McMaster University, Hamilton, Canada
3Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Canada
4Health Information Research Unit, McMaster University, Hamilton, Canada
5Department of Medicine, McMaster University, Hamilton, Canada
6Canadian Blood Services, Hamilton, Canada

Background: Antibodies of undetermined significance/specificity (AUS) are often detected when using a solid-phase platform, in part due to increased sensitivity. AUS are resource intensive and may delay transfusions. There is a paucity of literature surrounding the incidence, natural history, and patient factors associated with AUS. This study aims to determine the frequency of AUS detected using solid-phase technology; report on reflective laboratory testing; and identify patient factors associated with positive AUS results.

Study Design/Methods: A 1-year retrospective review of Transfusion Medicine Laboratory antibody records was conducted at a large academic institute. All patients with an antibody screen were included in the study. Laboratory test results and patient factors, including age, sex, ABO, Rh type, transfusion history, and subsequent antibody formation, were extracted from a network of databases.

Results/Findings: AUS were detected in 720 (1.9%) patients and 1,956 (3.5%) samples. The frequency of AUS was significantly higher in female patients (2.2%) compared to males (1.5%); absolute difference 0.7%, 95% CI (0.4%-0.9%); (p<0.0001). The average number of tests conducted relating to antibody-investigation was higher for patients with AUS. Patients with an alloantibody were ~7 times more likely to have coexisting AUS, and the frequency of AUS and anti-E was most common.
**Conclusion:** AUS are more frequently seen in females and lead to increased testing and use of resources. Additional investigations are required to elucidate natural history, associated patient factors, and clinical significance of AUS.

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**Therapeutic targeting of impaired lysosomal flux in Alzheimer’s disease**

A Somogyi1,4, A Frizzati2, R Sims2, E Lloyd-Evans3, B Boland4, C O’Neill1

1School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland
2School of Medicine, Cardiff University, Cardiff, UK
3School of Biosciences, Cardiff University, Cardiff, UK
4Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland

The deposition and spread of β-amyloid (derived from amyloid precursor protein(APP)) and tau are the two major pathogenic hallmarks of Alzheimer’s disease (AD). However, an increased number of enlarged neuronal endocytic compartments, whose origin remains elusive, precedes this AD pathology. We hypothesise that pathogenic changes in TRPML1 activity, a lysosomal Ca2+ release channel, essential for fusion and degradation of endosomal and autophagic cargo, may underlie this early endocytic pathology causing a build-up of Aβ and tau in AD. This is supported by the realisation that many late-onset AD risk genes regulate or directly bind to the endogenous modulators of TRPML1, the phosphoinositides PI(3,5)P2 and PI(4,5)P2. Therefore, the central objective of this study is to investigate the integrity of the TRPML1/phosphoinositide regulated network in AD brain at different stages of severity, and to determine if targeting TRPML1 using synthetic agonists can protect against both Aβ and tau pathogenesis. Our preliminary data indicate that defects in the TRPML1 system occur in the brain of AD patients. Furthermore, rat primary cortical neurons were treated with YM201636 to deplete cells of the endogenous lipid agonist of TRPML1, PI(3,5)P2. YM201636-treated neurons developed endosomal-autophagic enlargement, resembling that observed in pre-symptomatic AD. Treatment of YM201636-treated neurons with ML-SA1, a synthetic TRPML1 agonist, rescued this pathology. Furthermore, TRPML1 activation with ML-SA1 decreased levels of both hyperphosphorylated tau and full-length APP, while increasing levels of C-terminal fragments derived from non-amyloidogenic α-secretase cleavage of APP. Together these results indicate the potential use of TRPML1 agonists as novel therapeutic targets for AD.
Demonstrating the potential benefit of palliative care input for people living with dementia, using case studies

S Fox¹, S Cahill², MJ Foley², M Lynch³, S Timmons¹

¹Centre for Gerontology and Rehabilitation, School of Medicine, University College Cork, Cork, Ireland
²Assessment and Treatment Centre, St Finbarr's Hospital, Cork, Ireland

Introduction: Although dementia is a life-limiting illness, it is often not recognised in this way. People with dementia, and their carers, have been shown to have palliative care needs equal to those of cancer patients. Although palliative care is recognized as quality care at end-of-life, palliative care for people with dementia is still evolving.

Aim: To demonstrate the benefit of a palliative care approach for people with dementia, through case studies.

Methods: We conducted 6 case studies with people with dementia and their families. We used quantitative (questionnaires) and qualitative (interviews) data to explore their palliative care needs, and potential benefit of SPC input.

Results: Caring for a loved with dementia is very difficult, carers experienced high levels of anxiety, depression, and caregiving-burden. Carers wanted more emotional support, and felt that sometimes they were not included in the unit of care. Carers found it difficult coping with transitions of care, especially when a decision was made to move the person with dementia into long term care. Many carers experienced anticipatory grief. In cases of young onset dementia (<65 years) their children can greatly benefit from emotional support.

Conclusion: People with dementia and their families could be greatly supported through a palliative care approach. Carers value formal psychological and emotional support, assistance with decision making about their loved one’s care needs, and advice on advance care planning.
Absence of the neurogenesis-dependent nuclear receptor TLX induces inflammation in the hippocampus

DA Kozareva¹, CM Hueston¹, CS O Leime¹, S Crotty¹, P Dockery², JF Cryan¹,³, YM Nolan¹,³

¹Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
²Department of Anatomy, National University of Ireland, Galway, Ireland
³APC Microbiome Institute, University College Cork, Cork, Ireland

The orphan nuclear receptor TLX (Nr2e1) is a key regulator of hippocampal neurogenesis. Impaired adult hippocampal neurogenesis has been reported in neurodegenerative and psychiatric conditions including dementia and stress-related depression. Neuroinflammation is also implicated in the neuropathology of these disorders, and has been shown to negatively affect hippocampal neurogenesis. To investigate a role for TLX in hippocampal neuroinflammation, we assessed microglial activation in the hippocampus of mice with a spontaneous deletion of TLX. Results from our study suggest that a lack of TLX is implicated in deregulation of microglial phenotype and that consequently, the survival and function of newborn cells in the hippocampus is impaired. TLX may be an important target in understanding inflammatory-associated impairments in neurogenesis.
P62

**Factors Associated with Influenza Vaccination Among Health Care Workers: A Cross-Sectional Study**

AM Liston

*Epidemiology and Public health, UCC, Cork, Ireland*

**Abstract**

**Objective:** the aim of the study was to explore factors which may be associated with influenza vaccination among Health Care Workers (HCWs).

**Design:** Cross-sectional observational study

**Setting:** Four community hospitals, two critical care units, eight public health centres, and five day care centres in the South of Ireland

**Participants:** 180 health care workers

**Methods:** Self-administered anonymous validated questionnaire

**Results:** Twenty-eight percent of respondents received the influenza vaccine. Forty-one percent of those that didn’t receive the vaccine refused due to fears of safety, (62% of which cited fear of developing influenza as a concern). Fourteen percent did not receive the vaccine due to inconvenience/no time. Eighty-one percent of these HCWs received information about the influenza vaccination from the Health Service Executive (HSE). Those that agreed that vaccinating HCWs helps to protect patients had an increased probability of receiving the vaccine. [OR = 3.88, p = .015, 95% CI = 1.29 – 11.6.]
Conclusions: Education to address misconceptions and misperceptions around influenza vaccination, as well as making the receipt of the vaccine more convenient, is needed to improve uptake among HCWs. As the majority of participants received their information from the HSE, there was disparity between the intended message and what had been interpreted or disregarded by HCWs indicating a need to adapt the current strategy of communicating information in order to debunk myths and promote vaccination as a means of self-protection.

P63

Bugs, Breathing and Blood Pressure: Intermittent Hypoxia Related Cardio-Respiratory Dysfunction in Rat

KM O'Connor1,2,3, EF Lucking1, JF Cryan2,3, KD O'Halloran1,3

1Department of Physiology, School of Medicine, University College Cork, Cork, Ireland
2Department of Anatomy and Neuroscience, School of Medicine, University College Cork, Cork, Ireland
3APC Microbiome Institute, University College Cork, Cork, Ireland

Obstructive sleep apnoea syndrome, a respiratory disorder characterised by exposure to chronic intermittent hypoxia (CIH), has maladaptive outcomes for integrative body systems. Aberrant cardiorespiratory plasticity occurs following exposure to CIH. CIH functions as a major driving force at the gut epithelium, leading to inescapable microbial diversity. We sought to explore the effects of CIH on major homeostatic control systems, with an interest in host-microbiome interactions, which may underpin the development of several cardiorespiratory morbidities.

Sprague Dawley adult male rats were exposed to repeated cycles consisting of hypoxia and normoxia for 8 hours per day for 2 weeks. Sham animals were subjected to the same environmental cues but were constantly exposed to room air. Using whole-body plethysmography, ventilation and metabolism were measured during air breathing and hypercapnia in unanesthetised, unrestrained animals at quiet rest. Under urethane anaesthesia, cardiorespiratory recordings and reflexes were examined.

Exposure to normoxia did not alter ventilation in CIH-exposed rats compared with sham. Short-term and long-term variability of respiratory timing was not different in CIH-exposed animals compared with sham. However, CIH exposure increased apnoea index during normoxia and hypercapnia. Alterations in sigh frequency during hypercapnia were also noted in CIH-exposed animals. Exposure to CIH increased mean arterial blood pressure.

Our study employing a CIH-exposed rat model of sleep apnoea reveals dysregulated cardiorespiratory control, which may result in whole-body health deterioration. Impaired cardiorespiratory homeostasis may further disrupt microbial composition. Investigation
into the association between host-microbiome and cardiorespiratory homeostasis is required. Manipulating the microbiota may function as an adjunct therapy for the treatment of sleep-disordered breathing.

P65

Profile of patients presenting to emergency departments in the Southwest of Ireland following repeated episodes of self-harm

D Leahy1,2, G O'Regan1,2, E Cassidy3, J Kinahan4, C Corby5, M Clancy6, E Williamson2, A Arensman1,2

1Department of Epidemiology and Public Health, University College Cork, Cork, Ireland
2National Suicide Research Foundation, University College Cork, Cork, Ireland
3Department of Psychiatry, Cork University Hospital, Cork, Ireland
4Department of Psychiatry, Mercy University Hospital, Cork, Ireland
5Department of Psychiatry, University Hospital Limerick, Limerick, Ireland
6Department of Psychiatry, University Hospital Waterford, Waterford, Ireland

Introduction: Major repeaters are defined as patients with a history of 4 or more previous self-harm episodes. According to findings from the National Self-Harm Registry Ireland, among patients identified as major repeaters, 82% engaged in a repeated act of non-fatal self-harm in the 3 months following an index self-harm presentation to hospital. This study is being conducted as part of the five year Health Research Board funded project: Improving Prediction and Risk Assessment of Self-harm and Suicide (IMPRESS). The current paper will focus on baseline data from the major repeater group.

Methods: Consecutive patients presenting to emergency departments of two hospitals in Cork and one in Limerick, following a repeated self-harm episode were invited to participate in semi-structured interviews. All patients’ psychiatric assessments were reviewed to examine the representativeness of the interviewed sample.

Results: From August 2016-2017, 80 patients who presented to the emergency departments met the major repeater criteria and 24 patients participated in semi-structured interviews. The average age of the patients was 34 years and the majority were female (60%). The most common methods of self-harm were intentional drug overdose (57%) and self-cutting (30%). Based on findings from the interview data, 78% of participants had a history of ten or more self-harm episodes and 80% of participants had a history of physical, sexual or emotional abuse.
Conclusions: The high rates of previous self-harm episodes accompanied by equally high rates of abuse would suggest the need for specific treatment interventions for these patients to manage long-term engagement with services.

P66

USING A STANDING WORKSTATION DOES NOT ATTENUATE THE TIME-DEPENDENT DECLINE IN NEUROVASCULAR COUPLING RESPONSE MAGNITUDE

JK Leacy1,2, LR Lavoie2, EM Johnson2, DP Sheehan2, KD O’Halloran1, N Sharma3, TA Day2

1Department of Physiology, University College Cork, Cork, Ireland
2Department of Biology, Mount Royal University, Calgary, Canada
3Department of Physiology, University of Calgary, Calgary, Canada

Neurovascular coupling (NVC) is the regulation between neuronal metabolic demand and local cerebral blood flow. It remains unclear if decreasing sedentary behaviour (SD) time improves NVC responsiveness. We hypothesized that the adoption and use of a standing workstation would improve NVC responsiveness over six months.

Routinely sedentary working participants (39.75±9.9yrs) were sub-divided into Control (no standing workstation; n=15) and Intervention (standing workstation; n=17) groups. Sitting and standing behaviour was measured via accelerometer (ActivPal) at zero and six months. NVC in the posterior cerebral artery (PCA) was elicited and measured via transcranial Doppler ultrasound and a standardized visual stimulation (strobe light; 6Hz; 30sec on/off x5) at 0 and 6 months. A mean change in peak PCA velocity from baseline (ΔP) was calculated during visual stimulation.

No significant change in sitting or standing behaviour was observed in the Control group (P>0.56). In the Intervention group, a significant decrease in sitting (P<0.001; mean 17.95 ± 14.89%) and increase in standing behaviour (P<0.001; mean 16.05 ± 15.15%) was observed from 0-6 months. There was a significant decrease in ΔP in both the Control (P=0.004) and intervention (P<0.001) groups from 0-6 months.

Our results demonstrate (a) a significant reduction in NVC responsiveness over six months and (b) replacing <20% of time spent sitting with standing in the workplace, is not a sufficient enough intervention to preserve NVC responsiveness or reverse the decline over the short-term. Future studies should investigate the effect of other
modalities designed to reduce SD, and their impact on preserving NVC responsiveness over longer durations.

P67

Regulatory considerations for gene therapy design

A Hilliard¹,², M Tangney¹,²,³

¹Cork Cancer Research Centre, University College Cork, Cork, Ireland
²SynBioCentre, University College Cork, Cork, Ireland
³APC Microbiome Institute, University College Cork, Cork, Ireland

Gene therapy medicinal products (GTMPs) have emerged as an exciting platform technology for the treatment of a vast number of diseases. Typically, gene therapies are designed and developed within academic centres for whom regulatory issues are rarely considered. The regulatory framework surrounding GTMPs is complex and represents a significant challenge for academic centres which lack the human and financial resources for developing pharmaceutical products to a marketable state. The biotechnology industry subsequently undertakes to sponsor clinical trials for the most promising gene therapies. As a result, clinical trials are carried out with insufficiently developed products which consequently require changes to its design to adhere to the strict regulatory requirements and guidelines set by the relevant authorities.

Another significant challenge in GTMP design is that a relatively small number of GTMPs have been assessed by the regulatory authorities such as the EMA (European Medicines Agency). Consequently, the regulations governing this type of product are quite undeveloped. In particular, gene therapies which utilise genetically modified organisms as a vector present unique challenges with regards to infection control issues. Therefore, those developing GTMPs must consider the wider implications of the products on the general public and the environment in order to address any potential safety issues which may be a regulatory concern.

Here we examine the current regulatory requirements that researchers should consider when designing a gene therapy to ensure compliance with current guidelines.
Investigating the association between long non-coding RNAs and ductal carcinoma in situ (DCIS)

J Samson¹, S Das², D O'Connor², C Murphy³, A O'Shea³, MB Casey³, K Dean¹

¹School of Biochemistry and Cell Biology, UCC, Cork, Ireland
²Department of Molecular and Cellular Therapeutics, RCSI, Dublin, Ireland
³Bon Secours Hospital and School of Medicine, UCC, Cork, Ireland

Breast cancer is the most common cancer in women globally, with incidence rates increasing and survival rates varying widely depending on early detection and access to treatment. In Ireland, the number of diagnoses is increasing (National Cancer Registry, 2016), with 89% of new cases being invasive breast cancer. To reduce the number of individuals with invasive cancer, there is an urgent need for specific and sensitive diagnostic biomarkers for the earliest stages of breast cancer.

Ductal carcinoma in situ (DCIS) is a non-obligate precursor to invasive ductal carcinoma. With an increasing number of studies linking long, non-coding RNAs (lncRNAs) to various cancers, we have specifically selected to examine lncRNAs as novel DCIS biomarkers and to characterise their biological roles. Here, we present RNA sequencing results from two DCIS patient-derived cell lines, identifying several lncRNAs with altered expression. Expanding this to our DCIS patient cohort, we will use sequence capture technology, coupled with next-generation sequencing, to identify lncRNAs, correlate lncRNA signatures with clinicopathological features and refine our focus to clinically-relevant lncRNAs for further study. In parallel, we are investigating the role of BC200, a lncRNA associated with high, nuclear-grade DCIS. By altering the levels of BC200 in DCIS cell lines experimentally, we aim to characterize how BC200 affects DCIS cell behavior through a series of cell-based assays. Ultimately our goal is to identify and characterise lncRNA biomarkers in DCIS, leading to the development of diagnostic tools that could change how early breast cancer is detected and treated in patients worldwide.
Development of a Click Beetle Luciferase Reporter System for Enhanced Bioluminescence Imaging of Listeria monocytogenes: Analysis in Cell Culture and Murine Infection Models

S Ur Rahman1,2,3, RM Stanton4, P Casey1, A Spagnuola5, G Bensi5, C Hill1,2, KP Francis6, M Tangney1,4,7, CGM Gahan1,2,78

1APC Microbiome Institute, University College Cork, Cork, Ireland
2School of Microbiology, University College Cork, Cork, Ireland
3College of Veterinary Sciences and Animal Husbandry, Abdul Wali Khan University Mardan, Mardan, Pakistan
4Cork Cancer Research Centre, University College Cork, Cork, Ireland
5GSK Vaccines S.r.l, Siena, Italy
6PerkinElmer, Almeda, CA, USA
7SynBio Centre, University College Cork, Cork, Ireland
8School of Pharmacy, University College Cork, Cork, Ireland

Listeria monocytogenes is a Gram-positive facultative intracellular pathogen that is widely used as a model organism for the analysis of infection biology. In this context, there is a current need to develop improved reporters for enhanced bioluminescence imaging (BLI) of the pathogen in infection models. We have developed a click beetle red luciferase (CBR-luc) based vector (pPL2CBRopt) expressing codon optimized CBR-luc under the control of a highly expressed Listerial promoter (PHELP) for L. monocytogenes and have compared this to a lux-based system expressing bacterial luciferase for BLI of the pathogen using in vitro growth experiments and in vivo models. The CBR-luc plasmid stably integrates into the L. monocytogenes chromosome and can be used to label field isolates and laboratory strains of the pathogen. Growth experiments revealed that CBR-luc labeled L. monocytogenes emits a bright signal in exponential phase that is maintained during stationary phase. In contrast, lux-labeled bacteria produced a light signal that peaked during exponential phase and was significantly reduced during stationary phase. Light from CBR-luc labeled bacteria was more efficient than the signal from lux-labeled bacteria in penetrating an artificial tissue depth assay system. A cell invasion assay using C2Bbe1 cells and a systemic murine infection model revealed that
CBR-luc is suited to BLI approaches and demonstrated enhanced sensitivity relative to lux in the context of Listeria infection models. Overall, we demonstrate that this novel CBR reporter system provides efficient, red-shifted light production relative to lux and may have significant applications in the analysis of L. monocytogenes pathogenesis.

P70

Glial-mediated clearance of extracellular autophagic-lysosomal organelles generated by cultured neurons: Relevance to Alzheimer’s Disease

AV Jaisimha², S Hegarty², CJ Dunworth², K Phelan², D Walsh¹, B Boland²

¹School of Biomedical and Biomolecular Science, University College Dublin, Dublin, Ireland
²Pharmacology and Therapeutics, University College Cork, Cork, Ireland

Background: Altered catabolism of amyloid precursor protein (APP) and tau is widely implicated in the pathogenesis of Alzheimer’s disease (AD). Lysosomal flux refers to the catabolic clearance of autophagic and endocytic cargo by lysosomes, which is known to be impaired in AD.

Methods: Two different neuron culture models were used, namely, (i) neuron-enriched rat primary cortical neuron cultures and (ii) neuron-glia mixed cultures. In vivo analysis of human post-mortem brain tissue from AD and age-matched non-demented control brain tissue was also performed.

Results: The specific lysosomal proteases, cathepsin L and B, were found to regulate the turnover of APP C-terminal fragments (CTFs) within cultured neurons and their pharmacological inhibition caused a preferential accumulation of novel truncated APP-CTFs, which was indicative of impaired lysosomal flux. Levels of lysosomal APP-CTFs and the autophagic vacuole marker, LC3-II, did not differ between control AD brain tissue. However, large extracellular vesicles (>1μm) purified from conditioned media from neuron-enriched cultures, were found to contain neuron-specific βIII-tubulin, LC3-II, APP-CTFs and phosphorylated tau. Depletion of these markers in conditioned media from neuron-glia cultures indicated glial cells mediate the uptake and clearance of neuron-derived extracellular vesicles of autophagic-lysosomal origin.

Conclusions: Lysosomal flux is a process mainly been associated with the clearance of intracellular cargo. Evidence of impaired lysosomal flux is present at the ultrastructural level in post-mortem AD tissue, yet biochemical markers of this pathology remain elusive. Findings from this study suggest that neurons avoid the accumulation of
lysosomal cargo by secreting intact organelles, which are cleared by glial cells. Applications of this in vitro model may be useful for identifying factors that modulate the secretion of neuron-derived lysosomal organelles in the AD brain.

P73

Does daily consumption of vitamin K1 from cruciferous vegetables reach the circulation?

SM O'Sullivan¹, K Galvin¹, R Davidson², I Clark², A Lucey¹

¹School of Food and Nutritional Sciences, University College Cork, Cork, Ireland
²School of Biological Sciences, University of East Anglia, Norwich, UK

Cruciferous vegetables, such as broccoli, cabbage and kale, contain high quantities of vitamin K1. Vitamin K1 acts as an enzyme co-factor which carboxylates vitamin K-dependent proteins that have been implicated in osteoarthritis (OA) and other diseases of aging. OA is the most prevalent joint disorder in older adults and is a major cause of disability. Studies have suggested that low vitamin K1 status is associated with a higher incidence of OA. This study investigated the levels of vitamin K1 in plasma following a broccoli-based dietary intervention in adults with knee OA undergoing total knee replacement. The main aim of this study was to evaluate whether 100 g of broccoli per day can increase vitamin K1 status, which in turn may aid in the development of public health strategies to increase vitamin K1 status at population level. This proof-of-principle, randomised parallel-design trial enrolled 40 patients with knee OA undergoing total knee replacement. Participants underwent a washout period for 7 days where cruciferous vegetable consumption was limited. Participants were then randomised to either increased broccoli consumption (100g of cooked broccoli/day) or no broccoli consumption for 7 days prior to surgery. Vitamin K1 concentrations were measured in plasma at baseline and post-intervention by reversed phase (RP)-HPLC.
The development of a Suicide and Self-Harm Observatory (SSHO) in Ireland

R Benson¹, J Rigby², E Arensman¹,³

¹School of Public Health, National Suicide Research Foundation, Cork, Ireland
²National Centre of Geocomputation, Centre for Health Geoinformatics, Maynooth, Ireland
³School of Public Health, University College Cork, Cork, Ireland

The process of verification, registration and classification of external causes of death, including suicides in Ireland usually involves several months and in some cases up to two years due to the requirement of a Coronal inquest and the involvement of an Garda Síochana, pathologists, and registrars. A reliance on mortality statistics published by the CSO two years after the calendar year in which they took place results in delays of reviews and modifications to suicide prevention plans. Having access to a real-time surveillance system which can be measured against CSO statistics will assist in the prevention of further suicide and self-harm cases during this period and improve early identification of emerging suicide and self-harm clusters.

Building on the Suicide Support and Information System, which accesses information relating to consecutive cases of suicide and open verdicts upon completion of a coronial inquest, the Suicide and Self-Harm Observatory (SSHO) has been developed with the aim to obtain minimal data on suspected suicide cases from the Coroners (in advance of inquest), an Garda Síochana, the HSE patient mortality and the National Self-Harm Registry Ireland on a real-time basis. Methodological and ethical aspects of the development of the SSHO will be addressed.

Data obtained by the SSHO will increase the capacity for early intervention when potential suicide and self-harm clusters are identified and facilitate implementation or activation of local plans to respond to emerging clusters. In addition, the SSHO will assist with optimising resource allocation and inform health service responses in geographical areas with recurring clusters.
In situ bacterial production of therapeutic antibody fragments

VVB Yallapragada\textsuperscript{1,2}, C Devoy\textsuperscript{1,2}, M Tangney\textsuperscript{1,2,3}

\textsuperscript{1}Cork Cancer Research Centre, University College Cork, Cork, Ireland
\textsuperscript{2}SynBioCentre, University College Cork, Cork, Ireland
\textsuperscript{3}APC Microbiome Institute, University College Cork, Cork, Ireland

The therapeutic potential of antibodies has undergone unprecedented scientific and commercial development in the last 20 years. Due to the rise of engineered antibody fragments such as ScFVs, diabodies, Bi-specific T-cell Engagers (BiTE), tri-specific fragments, etc., therapeutic antibodies have gained wide attention in recent times. Designing such semi-customized antibody fragments against one or more epitopes needs an interdisciplinary approach to translate the \textit{in silico} aided design into a potential therapeutic. Today, with the availability of protein engineering and synthetic biology tools, the ‘design, model, build and test’ of these fragments is rapidly accelerating and reducing the cost and time of research. However, some properties such as pharmacokinetics, bioavailability, half-life and antigenicity are also dependent on the production and delivery platform used.

Bacteria have been a widely used production platforms. Given the natural ability of bacteria to selectively grow within tumours, they could conceivably form the final ‘drug’ product for administration, to provide \textit{in situ} production of the therapeutic. \textit{In silico}-aided, \textit{in situ} delivery of bacterial-produced synthetic antibody fragments has exciting potential to deliver therapeutics locally, thus solving the problems associated with antibodies such as bioavailability, and reducing side effects.

In the present work, we demonstrate \textit{in silico} aided design and \textit{in vitro} testing of monovalent ScFVs, mono-specific bi-valent diabodies and bi-valent BiTEs against hHER2, hMucin1 and mCD3 antigens.
Limitations in the use of Iron Indices as Markers for Iron Overload

A O’Brien, B Kerr, C Joyce

Clinical Chemistry Dept., Cork University Hospital, Cork, Ireland

Introduction: Hereditary Haemochromatosis (HH) is an autosomal recessive disorder of iron metabolism caused by mutations in the HFE gene. It is a common disorder in Northern Europeans affecting one in 200-300 individuals. The HH investigation protocol involves measurement of fasting transferrin saturation (%TS) with a cut off value of 45% required for genetic testing. %TS is calculated from serum iron and transferrin concentration. Serum iron is subject to diurnal variation and transferrin is a negative acute phase protein (APP) therefore both variables will affect the calculation of %TS. Ferritin, a positive APP is often used in the initial screening of patients for HH testing.

Aim: Retrospectively interrogate the laboratory database for iron indices and inflammatory markers in patients referred for HH genetics over a 2 year period.

Methods: A search of the laboratory information system (LIMS) using Cognos software was performed. Results were obtained for the following biomarkers; iron, transferrin, %TS, Ferritin and CRP. A cohort of patients with %TS>45% and low transferrin levels were selected for further study.

Results: The percentage of patients referred for genetic testing on the basis of high %TS and low transferrin levels was calculated. The majority of these patients had a wild type genotype. Results thus indicate over-investigation of HFE genotype in cases of low TF with high %TS.

Conclusion: Use of %TS as a marker of iron overload should be used with caution in the setting of a low transferrin. Inclusion of an interpretive comment may be necessary to alert clinicians.
Isolation of Virus-Free Antigen Binding Fragments (VF-FAbs) from Antibody-Associated Hepatitis C Virus

NE Walsh¹, A Naik¹, C De Gascun², B Palmer¹, E Kenny-Walsh³, O Crosbie³, C O'Farrelly⁴, LJ Fanning¹

¹Molecular Virology Research and Diagnostics Laboratory, University College Cork, Cork, Ireland
²National Virus Registry Laboratory, University College Dublin, Dublin, Ireland
³Department of Gastroenterology, Cork University Hospital, Cork, Ireland
⁴School of Biochemistry and Immunology, Trinity College Dublin, Dublin, Ireland

Introduction/Background: The genetic diversity of the hepatitis C virus (HCV), combined with selective pressure from host defence mechanisms, creates an environment that produces numerous HCV variants – these viral variants circulate throughout the human host as a ‘quasispecies’ population. This population mutates to evade antibodies generated by the host, leaving the host unable to combat the infection. Analysis of serum taken from infected HCV patients has revealed the presence of antibody-associated virus (AAV).

Methodology: Thirteen HCV serum samples were received from the National Virus Registry Laboratory (NVRL) and screened using a combination of column chromatography and RT-PCR for the presence of AAV. Four positive (AAV(+)) and nine negative (AAV(-)) samples were identified. The AAV(+) samples underwent a proteinase K digestion to remove the virus from the antibody-virus complex. Further column chromatography and RT-PCRs generated two ‘virus-free antigen-binding fragments’ (VF-FAbs). The two VF-FAbs were used to ‘challenge’ the AAV(-) samples – this was done through the incubation of the VF-FAbs and the AAV(-) samples at 37°C for two hours. RT-PCR was used to verify whether the VF-FAbs had bound to the virus.
**Results:** Two VF-FAbs (VFF-C and VFF-G) were isolated from the AAV+ samples. VF-FAb ‘challenges’ against the AAV(-) samples showed that the VF-FAbs were unable to capture HCV. Phylogenetic analysis was carried out to determine the relatedness of the AAV(+) and AAV(-) samples.

**Conclusion:** The VF-FAbs were unable to capture unrelated HCV. The AAV(-) samples did not share common epitopes with the AAV(+) samples that the VF-FAbs were isolated from.

**P78**

**Non-receptor tyrosine kinase FER enhances Insulin-like Growth Factor-1 Receptor activation to promote an aggressive cancer phenotype.**

JS Stanicka¹, LR Rieger¹, SOS O'Shea¹, MC Coleman¹, OC Cox¹, COF O'Flanagan¹, JB Berghoff¹, BA Addario¹, RK Kennedy², ROC O'Connor¹

¹School of Biochemistry and Cell Biology, University College Cork, Cork, Ireland
²Centre for Cancer Research and Cell Biology, Queens University, Belfast, Northern Ireland

The Insulin-like Growth Factors promote cancer progression by acting through a cell surface tyrosine kinase receptor (IGF-1R). Activity of this receptor can be modulated in cancer cells to develop an aggressive phenotype. The aim of this study was to discover cellular proteins that modify IGF-1R activity in cancer cells and determine the mechanism of action. We identified the non-receptor tyrosine kinase FER as a mediator of sensitivity to IGF-1R kinase inhibitors. This suggested that FER modulates IGF-1R activity. To test this we suppressed and ectopically expressed FER in different cell lines. FER silencing greatly reduced IGF-1R levels, which lead to an impaired cell proliferation and IGF-1-promoted cell migration. Ectopic FER expression enhanced IGF-1R stability and its expression levels at both plasma membrane and sites of focal cell adhesion. FER significantly increased IGF-1R autophosphorylation and IGF-1-induced SHC phosphorylation leading to MAPK pathway activation. The effects of FER on the IGF-1R require the association of the IGF-1R and β1 Integrin at focal adhesion points. High FER expression in breast cancer patients correlates with poor prognosis and a mesenchymal/aggressive phenotype. We conclude that FER-enhanced IGF-1R stability and signalling promotes cancer progression, which makes it an attractive therapeutic target.
Expression of p40 versus p63 in Cutaneous Squamous Cell Carcinoma and Cutaneous Spindle Cell Malignancies

M Dorney¹, R Werner¹, CC Heffron¹,²

¹Department of Pathology, Cork University Hospital, Cork, Ireland
²UCC Department of Pathology, Cork University Hospital, Cork, Ireland

Cutaneous spindle cell tumours and in particular poorly differentiated sarcomatoid and spindle cell squamous cell carcinoma (SCC) can present a diagnostic challenge histologically due to similarities in their morphology and loss of marker expression. Identification of immunohistochemical markers that could be used in their distinction is vital given that the diagnosis can range from atypical fibroxanthoma to melanoma. The new monoclonal antibody p40 has been reported to have a higher specificity than p63 for detection of lung SCC but there are conflicting reports in the case of cutaneous SCC.

This study aims to resolve this conflict and compare the sensitivities and specificities of p63 and p40 in a range of cutaneous spindle cell lesions and cutaneous SCC of varying grades of differentiation. Immunohistochemistry for p63, p40, MNF116 and CD10 was examined on a cohort of 177 cases of atypical fibroxanthoma (n=25), leiomyosarcoma (n=9), desmoplastic melanoma (n=30), basal cell carcinoma (n=30) and SCC (n=83, ranging from well to poorly to spindle cell / sarcomatoid SCC).

100% of SCCs were p40 and p63 positive with p40 showing greater specificity (100% v 81%). Expression of p63 was noted in a number of cases of AFX, LMS and DM, a number of which had 50% of cells staining, while p40 expression was found in rare cells in only 2/25 cases of AFX. These results would support the use of p40 over p63 for the
P82

Knowledge, attitudes and beliefs of parents regarding adolescent human papillomavirus (HPV) vaccination: a systematic review and meta-ethnographic synthesis of the qualitative literature.

S Marshall¹, A Fleming¹, ², AC Moore¹, ³, LJ Sahm¹, ²

¹Pharmaceutical Care Research Group, School of Pharmacy, University College Cork, Ireland
²Department of Pharmacy, Mercy University Hospital, Cork, Ireland
³Department of Pharmacology and Therapeutics, University College Cork, Cork, Ireland

Background: Human papillomavirus (HPV) vaccination rates worldwide remain sub-optimal. The purpose of this research is to systematically review and analyse the qualitative literature on the parental knowledge, attitudes and beliefs regarding adolescent HPV vaccination, to achieve a greater understanding of the drivers and barriers to vaccine acceptability and to determine targets for a theoretically informed, evidence-based intervention to improve uptake.

Data sources: MEDLINE, CINAHL, EMBASE (from inception to December 2016), as well as grey literature and reference lists to identify primary qualitative literature.

Review methods: The seven-step model of meta-ethnography, described by Noblit and Hare, which uses a process of comparison and cross-interpretations between studies, while preserving the context of the primary data.

Results: Of 1759 citations identified, 71 were reviewed in detail and 33 were included, compiling the opinions of 1280 parents, in 14 different countries. Five key concepts that reflected the principal findings of all studies were determined: Is prevention better than cure?; The fear of the unknown; Limited knowledge and understanding; Complex vaccination decisions and; Parental responsibility.
**Conclusions:** The majority of parents are motivated to protect their children and prevent disease by accepting vaccines. Unlike other paediatric and adolescent vaccines, the link to sexual intercourse associated with the HPV vaccine often complicates the vaccination decision. Vaccine manufacturers, national healthcare systems and providers can reinforce the importance of immunisation and reiterate the rationale behind vaccination recommendations, by providing unambiguous information in a timely manner, transparently addressing parental concerns regarding vaccine safety and efficacy, whilst taking account of cultural and religious sensitivities and varying health literacy levels.

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**P84**

**Markers of apoptosis and autophagy are predictive of survival in oesophageal adenocarcinoma.**

S ElMashed¹, TR O'Donovan², E Kay¹, T O'Grady¹, D McManus³, S McQuaid⁴, R Turkinhton⁵, S McKenna²

¹Department of Histopathology, Beaumont Hospital, Dublin, Ireland  
²Cork Cancer Research Centre, UCC, Cork, Ireland  
³Department of Pathology, Belfast City Hospital, Belfast, Ireland  
⁴Northern Ireland BioBank, Centre for Cancer Research and Cell Biology, Belfast, Ireland  
⁵Centre for Cancer Research and Cell Biology, Queen's University Belfast, Belfast, Ireland

**Background:** Less than 20% of patients with advanced oesophageal carcinoma benefit from receiving neo-adjuvant therapy. Studies using oesophageal cancer cell lines have shown that drug sensitive tumour cells undergo apoptosis in response to drug treatment, whereas resistant cells induce autophagy and can recover following withdrawal of drug. In this study, we evaluated markers of apoptosis (cleaved/activated caspase 3) and autophagy (LC3B) to establish whether these markers are predictive of clinical response post neoadjuvant therapy.

**Methods:** Oesophageal adenocarcinoma tumour tissue from the Northern Ireland Biobank at Queens University Belfast was examined retrospectively. Tumors from 144 patients post neo-adjuvant therapy were assembled into tissue microarrays prior to immunohistochemical analysis. Kaplan-Meier survival curves and log-rank tests were used to assess the impact of active caspase 3 and LC3B expression on survival. Cox regression was used to examine association with clinical risk factors.

**Results:** In patients who received neo-adjuvant chemotherapy 38.9% had high LC3B expression, which correlated with poor overall survival (P=0.017). Conversely high
levels of active caspase 3 were found in 14.6% of patients and this correlated with a significantly better prognosis (P=0.027). A distinct globular pattern of LC3B expression was found to be predictive of overall survival (p<0.001).

**Conclusions:** The activation of caspase 3 and elevation of LC3B can provide pharmacodynamic markers of cellular response (apoptosis or autophagy) and outcome following neo-adjuvant treatment. In addition, a distinct globular LC3B staining pattern was observed as a highly predictive poor prognostic marker.

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**P85**

**High Concordance of BRAF Mutational Status by Molecular and Immunohistochemical Methods between Melanoma Primary and Metastases**

D Cormican¹, C Kennedy¹, S Murphy¹, R Werner¹, DG Power², CC Heffron¹,³

¹Department of Pathology, Cork University Hospital, Cork, Ireland.
²Department of Medical Oncology, Cork and Mercy University Hospitals, Cork, Ireland.
³UCC Department of Pathology, Cork University Hospital, Cork, Ireland.

Techniques for the accurate and efficient identification of activating mutations of the BRAF oncogene in metastatic melanoma are of great clinical importance, due to the availability of targeted therapies specific for these mutants. There is uncertainty regarding the frequency with which BRAF status differs between primary and metastatic sites, with discordance rates of 0 to 16% reported in previous series. This creates debate regarding whether the primary tumour or the metastases should be tested to determine future treatment. The aim of our study was to report our experience in Cork and compare our findings with those in the published literature.

Between 2011 and 2016, 219 melanoma cases underwent BRAF testing in our institution. In 53 of these, paired primary and metastatic specimens were available. BRAF mutational status was confirmed by COBAS 4800 RT-PCR testing and BRAF V600E immunohistochemistry at one site for all of these cases.

52 out of 53 cases (98%) showed concordant BRAF status between primary and metastatic site, with only one discordant case in which the primary tumour tested positive for BRAF V600E and the metastases was negative. However, following isolation of the small metastatic deposit and repeat molecular testing, it was found to be positive, thus 100% concordance was demonstrated.
The results suggest that discordance of BRAF mutational status between primaries and metastases is a rare occurrence. Our findings suggest that possible causes of discordance may be technical rather than a true mutational difference.

P86

The primary cilium in the CNS: an organelle of stress-related psychiatric disorders and antidepressant action?

V Novelli1, BR Levone1, JF Cryan1, 2, OF O’Leary1, 2

1Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
2APC Microbiome Institute, University College Cork, Cork, Ireland

Cilia are hair-like organelles protruding from the surface of most mammalian cell types including neurons. While motile cilia are involved in the generation of flow or movement, primary cilia are immotile and thought to function as sensory organelles. Intriguingly, primary cilia modulate many of the neuronal processes that have been implicated in the response to stress and antidepressants. Moreover, we previously found that the density and/or length of these structures in the medial prefrontal cortex area of the brain is reduced by chronic stress. The aim of the present study was to determine whether the stress hormone corticosterone and the antidepressant fluoxetine affect the density and length of primary cilia in neurons from brain regions implicated in the stress response and antidepressant action.

Rat hippocampal and cortical neurons were isolated, allowed to mature for 4 DIV and then treated with either corticosterone or fluoxetine. The highest concentration of corticosterone decreased both cilia density and length in hippocampal cultures, but also reduced cell viability. The highest concentration of fluoxetine decreased cilia length in hippocampal cultures and did not significantly affect cell viability or the density of ciliated cells. Dose-dependent effects of fluoxetine on the density and length of cilia were observed in cortical cultures but some effects were coupled with reduced cell viability. Taken together, these data suggest that non-toxic doses of corticosterone does not affect hippocampal primary cilia and that non-toxic doses of fluoxetine have limited effects on hippocampal and cortical primary cilia.
Role of specific sub-regions along the longitudinal axis of the hippocampus in the behavioural responses to chronic stress

BR Levone¹, JF Cryan¹,², OF O'Leary¹,²

¹Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
²APC Microbiome Institute, University College Cork, Cork, Ireland

The hippocampus is a key structure involved in learning, memory and stress-related psychiatric disorders including depression. Precisely how the hippocampus plays such seemingly diverse roles is not yet fully understood. However, accumulating evidence suggests that the hippocampus is functionally segregated along its longitudinal axis whereby the dorsal hippocampus (dHi) plays a predominant role in spatial learning and memory, while the ventral hippocampus (vHi) plays a predominant role in the regulation of anxiety a symptom often co-morbid with depression. Recent gene expression studies suggest that the area between the dHi and the vHi, the intermediate hippocampus (iHi) might also be functionally independent. However, the role of the dHi, iHi and vHi in the response to chronic stress, a risk factor for depression and anxiety disorders, has not yet been investigated. Thus, using ibotenic-induced lesions of these specific areas of the mouse hippocampus, we investigated the roles of the dHi, iHi and vHi in behavioural responses to chronic psychosocial stress. Interestingly, lesions of each of the three sub-regions prevented stress-induced increases in anxiety in several behavioural tests. None of the lesions affected stress-induced reductions in social interaction or anhedonic-like responses in the female urine sniffing test. On the other hand, some sub-region-dependent alterations in stress-induced anhedonia were observed in the saccharin preference test. Taken together, we suggest that although the vHi has been reported to have a preferential role in the regulation of anxiety, all hippocampal sub-regions are involved in the anxiogenic effects of chronic stress.
A marker panel consisting of LC3B, TRIM24 and Caveolin-1 predicts survival of oesophageal adenocarcinoma patients

S El-Mashed¹, TR O'Donovan², E Kay¹, MC Cathcart³, J O'Sullivan³, A O'Grady¹, J Reynolds³, SM McKenna²

¹Department of Histopathology, Beaumont Hospital, Dublin, Ireland
²Cork Cancer Research Centre, Western Gateway, University College Cork, Ireland
³Department of Surgery & Trinity Centre for Health Sciences, St James Hospital, Dublin, Ireland.

Aim: Expression patterns of the autophagy marker (LC3B) have been previously shown by this group to be associated with survival in oesophageal adenocarcinoma patients. In this study, we investigated the combined expression of LC3B, TRIM24 and Caveolin-1 as a predictive marker panel of patient outcome in oesophageal adenocarcinoma.

Materials and Methods: We performed immunohistochemical staining of LC3B, TRIM24 and Caveolin-1 on tumour tissue arrays of 84 chemo naïve oesophageal adenocarcinoma patients. Cox proportional hazard model and Kaplan-Meier survival curves were used to determine the relationship between markers and patients prognosis.

Results: LC3B cytoplasmic reactivity is associated with tumour differentiation (p=0.015), lymph node tumor metastasis (p=0.001), tumour pathological stage (p=0.001) and neural invasion (p=0.004). LC3B globular structures are only associated with lymph node tumour metastasis (p=0.013) and tumour pathological stage (p=0.003). There is a correlation between Caveolin-1 expression either in tumour cells or tumour stromal cell and tumour pathological stage and lymphatic metastasis. Each marker (LC3B, TRIM24 and Caveolin -1) predicts overall survival on univariate analysis. Positive for LC3B globular structures, TRIM24 expression and Caveolin-1 expression in tumour cells are
associated with poor prognosis (p=0.001, p=0.012 and p=0.005 respectively). While positive LC3B cytoplasmic expression and Caveolin-1 expression in tumour stromal cells are associated with better prognosis (p = 0.001 and p=0.005, respectively). A combined panel of the three markers increases the statistical significance (p-value) to <0.000.

**Conclusions:** We have identified a panel of three markers; LC3B, TRIM24 and Caveolin-1 that are predictive of patient outcome in oesophageal adenocarcinoma.

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**P89**

**Investigating a role for autophagy in ovarian cancer chemoresistance**

J Quinn, TR O’Donovan, SL McKenna

*Medicine and Health, Cork Cancer Research Centre, Cork, Ireland*

Ovarian cancer (OC) is the seventh most common gynaecological malignancy among women worldwide. In Ireland, ovarian cancer was the fourth most commonly diagnosed cancer among women between 1994 and 2010\(^1\). A major challenge in the clinical management of OC is the high rate of disease recurrence. Approximately 80% of women whom exhibit an excellent response to first line therapy present with recurrent disease, which is often more difficult to treat. We are investigating whether autophagy plays a role in this recurrance. Autophagy is a conserved catabolic process through which a cell recycles its own macromolecules and organelles following exposure to stress. This protects the cell and facilitates its recovery.

We have detected autophagy in ovarian cancer cells during their recovery from treatment with Paclitaxel, a drug commonly used in the clinical management of OC. Flow cytometry and western blot analysis of autophagy specific markers revealed an increase in autophagic vesicle accumulation. Immunofluorescence images have also shown colocalisation of autophagic vesicles and lysosomes following treatment with paclitaxel. Cell cycle analysis revealed the ability of OC cells to regain a ‘normal’ DNA profile following a seven day recovery period despite significant initial damage. siRNA knockdown of key autophagy genes will be performed to assess the impact of autophagy on this process. This work aims to provide a potential new therapeutic target, which could be used to combat chemoresistance in ovarian cancer.

1. National Cancer Registry Ireland

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\(^1\) National Cancer Registry Ireland
Psychotropic drugs modulate the gut microbiota in vivo

S Cussotto¹,², CR Strain¹,⁴, C Stanton¹,³,⁴, TG Dinan¹,³, JF Cryan¹,²

¹APC Microbiome Institute, University College Cork, Cork, Ireland
²Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
³Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland
⁴Teagasc Food Research Centre, Moorepark, Fermoy, Cork, Ireland

Psychotropic drugs are often associated with metabolic side effects. A growing body of evidence suggests that the gut microbiota plays a crucial role in controlling host physiology metabolism and behaviour, however the effects of certain psychotropic drugs on gut microbiota composition and intestinal permeability are currently unknown. The aim of this study was to investigate the impact of 3-week treatment with antidepressants and other psychotropic drugs on intestinal parameters and microbiota complexity/diversity in healthy rats.

To this end, seven experimental groups (vehicle, escitalopram, venlafaxine, fluoxetine, lithium, valproate and aripiprazole) received a 3-week treatment followed by assessment of locomotor activity, ex vivo intestinal permeability and microbiota sequencing. The antimicrobial activity of these drugs was also assessed in vitro. The data were analysed using one-way ANOVA followed by Dunnett’s t-test; all statistical analysis for microbiota sequencing were corrected for multiple comparisons.

None of the treatments influenced locomotor activity. Fluoxetine, lithium, valproate and aripiprazole increased the richness and diversity of gut microbiota species when compared to the vehicle-treated group. Ileum permeability was increased in escitalopram-, venlafaxine- and fluoxetine-treated groups, while there was no effect on colonic
permeability. Lithium and valproate treatment induced body weight loss that was accompanied with lower quantities of epididymal fat. *In vitro*, fluoxetine showed a dose-dependent antimicrobial activity against *B. longum* and *L. rhamnsosus*.

These data suggest that psychotropic drugs influence to some extent gut microbiota, intestinal permeability and host metabolism. Future research will investigate whether these gut-related effects play a role in the mechanism of action of these drugs.

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**P92**

**The Who, What, and Why of Drug Discovery**

G Hogan¹,², M Tangney¹,²,³

¹Cork Cancer Research Centre, University College Cork, Cork, Ireland  
²SynBioCentre, University College Cork, Cork, Ireland  
³APC Microbiome Institute, University College Cork, Cork, Ireland

The healthcare industry is experiencing a significant decline in R&D productivity, casting doubt on its sustainability, and provoking considerable inquiry into the prevailing forces at the root of the issue. General inquiry has been focussed on optimisation of technical, product-related R&D practices, with only brief consideration given to the people (or “actors”) by whom the institutionalisation of these practices is ultimately considered. We reason that R&D efficiency is dependent on an elegant understanding of the way inter-group relationships manifest within the field of drug discovery and development.

It has been shown that small-molecule drug discovery is dominated by big pharmaceutical companies. Further to this, we have shown that the discovery of “historically novel” therapeutics, like gene therapies, is avoided in larger companies. We suggest that this lack of initiative does not originate from a technical inability on big pharma’s part to execute historically novel drug discovery, rather that it originates from human behaviours that may be overcome in a people-centric way.

Big pharma’s disinclination towards historically novel drug discovery should be questioned in the context of an increasingly unproductive industry. To this end, we provide a case for why the involvement of actors of all types from the earliest stages of R&D can enhance R&D productivity and restore the industry’s viability, and discuss how confined, stereotypical perceptions of big pharma, small biotechnology companies, and academia can be disruptive to this.
Older Peoples’ Experiences of Attending Falls Risk Assessment Clinics in Primary Care

E Racine1, S Timmons2, PM Kearney1, S McHugh1

1Department of Epidemiology and Public Health, UCC, Cork, Ireland
2Centre for Gerontology and Rehabilitation, UCC, Cork, Ireland.

Background

A fall can negatively affect the confidence and independence of an older person living in the community. Listening to the voices of service users can improve the implementation of services to address the needs of those who are at risk of falling. Our aim is to explore older peoples’ experiences of attending new Falls Risk Assessment Clinics (FRAC’s) in primary care.

Methods

This is a concurrent mixed methods study. A quantitative survey was administered to those who attended the falls clinics and analysed using descriptive statistics. Eligible clients are those living in the community aged 65+ who are at risk of falls. Interviews were conducted with a purposive sample of service users (n=16) who agreed to be contacted during the survey. Thematic analysis was performed on qualitative data.

Results

The response rate for the survey was 60% (135/225). Sixteen people took part in the interviews. Overall, participants were satisfied with the assessment and support received. However, many felt the assessment was not enough to address their needs and they needed more follow up. There were also concerns regarding the lack of communication
between the clinics and GP’s. Practical obstacles to attending the clinic were identified such as insufficient parking facilities and unfamiliar clinic locations.

Conclusions

Older people who suffer a fall can be frail, vulnerable and therefore ‘hard to reach’ for research purposes. This study offers an opportunity for their voices to be heard. Their experiences will be used to inform and support ongoing implementation of the service.

P95

In silico design of synthetic therapeutic antibody fragments

VVB Yallapragada¹,²,⁴, E Da Silva Morais¹,²,³, SP Walker¹,², M Tangney¹,²,⁴

¹Cork Cancer Research Centre, UCC
²SynBioCentre, UCC
³Dept of Biological Sciences, Cork Institute of Technology
⁴APC Microbiome Institute, UCC

Recent advances in protein engineering has equipped us with the tools to design, modify and build various proteins for therapeutic purposes. In the last 30 years, the design of such complex and sophisticated proteins has been complimented by a parallel increase in the availability of computational resources and biological databases. However, the potential of in silico design is yet to be fully exploited. Antibody fragments are one such example of complex proteins. Several types of antibody fragments are currently being exploited by researchers for their therapeutic potential. Today, with predefined design requirement sets, a semi-customized antibody could be designed with existing computational tools. In the present work, we demonstrate the concept of in silico-aided design and how it could inform and guide wet lab experiments. Over 50 different models of various constructs of mono-valent ScFVs and bi-valent mono-specific diabodies against hMUC1 and hHer2 have been modelled and studied for their hydrophobicity, net surface charge, active site exposure and 3D structure. Appropriate solubility tags were added to the antibody fragments to reduce surface hydrophobicity. Linker types and sizes were optimized to find the right 3D conformation of the chains. Distances between the different affinity tags were adjusted to enable proper exposure of the active sites. Furthermore, to examine the binding of these constructs, the selected constructs were docked in silico onto their corresponding antigen to screen for the constructs with optimal functionality. We believe that such in silico aided design would be very useful and efficient approach to reduce wet lab efforts, cost and the time taken to conduct research.
Gut microbiota manipulation through caesarean section delivery alters hippocampal synaptic response

R O’Conor¹,², T Becker¹,², E Morelli¹,², T Dinan¹,³, JF Cryan¹,², H Schellekens¹,²

¹APC Microbiome Institute, University College Cork, Cork, Ireland
²Department of Anatomy & Neuroscience, University College Cork, Cork, Ireland
³Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland

Increasing evidence shows that microbiota composition affects neuronal structure and function. Recent experiments show altered myelination and dendritic morphology in germ-free animals. Additionally, modulation of the microbiota with antibiotics has been shown to lead to changes in anxiety-like behaviour & cognition in rodents. Interestingly, administration of probiotics has led to protective effects against age and diabetes-induced reductions in Long-term-potentiation in the hippocampus.

Gastrointestinal microbiota diversity and complexity is different in C-section-born subjects compared to vaginally-born subjects. In this project we investigated whether hippocampal samples from C-section animals had an altered electrophysiological signature.

A multi-electrode array was used to measure changes in electrical signalling in acutely-prepared hippocampal slices from mice delivered via c-section, or vaginally, 12-15 days postnatally. We then repeated experiments in the presence of the GABAa receptor antagonist, picrotoxin, to determine the role of GABAergic neurotransmission on the responses.

Electrophysiological readouts (input-output/ paired-pulse ratio) were altered in hippocampal preparations from C-section animals following GABAa blockade. Neurons
in slices from C-section animals showed reduced postsynaptic response following perfusion with picrotoxin as well as altered paired-pulse ratios.

Social behaviour was also assessed in adolescent mice. C-section delivery had an effect on social recognition but not social interaction in the three-chamber test. Dendritic morphology will be analysed at this age to determine whether these changes in behaviour may be linked to structural alterations.

These results suggest that mode-of-delivery has an effect on electrical signalling in the hippocampus though changes in GABA signalling onto glutamatergic neurons. Further experiments will investigate mechanisms underpinning these changes via oxytocin treatment in early life.

P97

Developing a Core Outcome Set of Infant Feeding Outcomes for Obesity Prevention Interventions

K Matvienko-Sikar¹, M Byrne², C Kelly³, E Toomey², M Hennessy², D Devane⁴, C Heary², J Harrington¹, N McGrath¹, M Queally⁵, PM Kearney¹

¹Department of Epidemiology & Public Health, University College Cork, Cork, Ireland
²School of Psychology, National University of Ireland Galway, Galway, Ireland
³School of Health Sciences, National University of Ireland Galway, Galway, Ireland
⁴School of Nursing and Midwifery, National University of Ireland Galway, Galway, Ireland
⁵Discipline of Economics, National University of Ireland Galway, Galway, Ireland

Background: Childhood obesity is a significant global public health challenge. Infant feeding practices are implicated in the aetiology of childhood obesity. Infant feeding interventions for childhood obesity are increasingly popular but outcome reporting is inconsistent across trials. Lack of standardisation limits examination of intervention effects and mechanisms of change. The aim of the current project is to develop a core set of infant feeding outcomes for children ≤ 1 year, to be evaluated in childhood obesity intervention trials.

Methods: An infant feeding core outcome set COS will be developed in four stages: (1) a systematic review of the literature, (2) discussion and clarification of outcomes identified in the systematic review, in a meeting involving multiple stakeholder perspectives, (3) prioritisation of outcomes using the e-Delphi technique with an expert panel of stakeholders, (4) achieving final consensus on the COS using the Nominal Group Technique consensus meeting.

Results: The systematic review identified 94 unique infant feeding outcomes within 9 outcome domains. Considerable heterogeneity was observed across all studies.
Clarification of outcomes and identification of additional outcomes was achieved in the stakeholder meeting. The e-Delphi study is ongoing.

**Discussion:** This study aims to develop a core outcome set of infant feeding outcomes for randomised infant feeding studies to prevent childhood obesity. This research will improve examination and syntheses of the outcomes of such studies to prevent and reduce childhood obesity.

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**P98**

**The CHErIsH Study: Developing primary care based pilot infant feeding intervention to prevent childhood obesity**

K Matvienko-Sikar, E Toomey, M Queally, M Byrne, C Heary, C Kelly, E Doherty, J Harrington, S McHugh, J McSharry, C Hayes, PM Kearney

1Department of Epidemiology & Public Health, University College Cork, Cork, Ireland
2School of Psychology, National University of Ireland Galway, Galway, Ireland
3Discipline of Economics, National University of Ireland Galway, Galway, Ireland
4School of Health Sciences, National University of Ireland Galway, Galway, Ireland
5Discipline of Public Health and Primary Care, Trinity College Dublin, Dublin, Ireland

**Background:** Childhood obesity is a serious public health concern. Early infant feeding practices are modifiable factors that can influence childhood overweight and obesity. The aim of this research is to develop, implement and evaluate an infant feeding intervention for childhood obesity.

**Methods:** This research is structured in 3 work packages. In Work-Package 1, quantitative and qualitative infant feeding literature is synthesised to form an evidence base. Work-Package 2 explores health service and stakeholder needs and experiences to inform selection of intervention components, methods, outcomes and objectives. This work package will also inform development of an intervention programme plan. Work package 3 involves implementing and evaluating the pilot intervention.

**Results:** A comprehensive evidence base of intervention effects, parental experiences of infant feeding, and parental and healthcare professionals’ experiences of intervention participation has been developed. The main output of Work-Package 2 is the development of a primary care based infant feeding intervention to prevent childhood obesity. Work-Package 3 will provide evidence on the effects of the intervention in a pilot trial, with concurrent economic and process evaluations.
Conclusion: This research approach will ensure the rigorous development of an appropriate, feasible and acceptable early infant feeding intervention for childhood obesity.

P99
Prevalence of Bendopnea in Systolic Heart Failure Patients

C Pray, D Kerins

1Medicine, University College Cork, Cork, Ireland
2Pharmacology and Therapeutics, University College Cork, Cork, Ireland

An estimated 23 million people worldwide suffer from heart failure (HF). The prevalence of HF has been steadily rising despite modern therapeutic innovations, and this trend is expected to persist. The diagnosis, and monitoring of those with HF requires continual clinical assessment of established symptoms and signs of HF. The European Society of Cardiology (ESC) published updated guidelines for the diagnosis and treatment of acute and chronic HF in 2016. In these guidelines a novel symptom of HF, bendopnea, was included. To date, there has been limited data published on this novel symptom, and there has been no data gathered that examines the prevalence bendopnea in patients with HF in an Irish population. This single centre prospective observational study utilized convenience sampling of individuals that attend the Department of Cardiology at the Mercy University Hospital in Cork, Ireland, and has the primary outcome of determining the prevalence of bendopnea in this population. Individuals with HF with reduced ejection fraction (LVEF ≤ 40%) were recruited and were provided with a modified Minnesota Living With Heart Failure Questionnaire (MLHFQ) through the post. This study additionally has a secondary outcome of determining whether there is a relationship between bendopnea and an individual’s quality of life in term of both the physical and psychological effects of heart failure. Data has been collected, and is currently undergoing statistical analysis for statistically significant results. Data analysis is expected to completed in the near future and at that point results, and study implications will be elaborated on.
Chronic intermittent hypoxia induced respiratory muscle dysfunction in adult male mice: a role for NADPH oxidase

S Drummond, DP Burns, KD O’Halloran

Department of Physiology, University College Cork, Cork, Ireland

Chronic intermittent hypoxia (CIH), a dominant feature of sleep-disordered breathing in humans, is considered a major driving force in the development of oxidative stress in a wide variety of tissues. The effects of CIH on respiratory muscles are relatively underexplored in mouse models. We sought to investigate a possible role for CIH induced NADPH oxidase (NOX) derived reactive oxygen species (ROS) in respiratory muscle dysfunction in mice.

Male C57/Bl6J mice (12 weeks) were exposed to normoxia (n=9) or 14 consecutive days of CIH (n=9) consisting of alternating cycles of normoxia (210s) and hypoxia (90s; 5% at the nadir) for 8 hours each day during light hours. An additional group of CIH treated mice (n=9) had free access to water containing Apocynin (2mm). Sternohyoid and diaphragm muscle isometric and isotonic contractile parameters were determined ex vivo.

Sternohyoid twitch (1.61 ± 0.40 vs. 1.12 ± 0.26 ** N/cm2) and tetanic force (9.40 ± 1.57 vs. 5.18 ± 1.36 *** N/cm2) force and diaphragm twitch (2.62 ± 0.89 vs. 1.63 ± 0.31* N/cm2) and tetanic force (22.63 ± 5.55 vs. 12.48 ± 2.32* N/cm2) were significantly reduced in CIH-exposed animals compared with normoxic controls. Pre-treatment with Apocynin prevented both sternohyoid and diaphragm muscle weakness. Values are mean ± S.D.

CIH caused profound sternohyoid and diaphragm muscle weakness, an effect prevented by pre-treatment with the putative NOX inhibitiior, Apocynin. Our results suggest that
respiratory muscle dysfunction in OSA may be due in part to NOX dependent oxidative stress and, as such, NOX inhibitors could potentially be useful as an adjunctive therapy for this disorder.

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P101

Analysis of comparable home / clinic blood pressure readings in the LEANBH population

E Roche\textsuperscript{1}, Y Lim\textsuperscript{2, 3}, L Kenny\textsuperscript{2, 3}

\textsuperscript{1}School of Medicine, University College Cork, Cork, Ireland
\textsuperscript{2}Department of Obstetrics and Gynaecology, University College Cork, Cork, Ireland
\textsuperscript{3}The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork, Ireland

Background:
Hypertensive disorders of pregnancy consist of a broad spectrum of conditions which are associated with significant negative outcomes for both mother and child. These disorders are common and are estimated to complicate 10-15\% of all pregnancies. Regular home blood pressure monitoring can be used as a way of identifying hypertension outside of the hospital clinic.

Aims and Objectives:
To determine the relationship between home and hospital blood pressure readings in a cohort of pregnant women.

Methods: This study used the LEANBH (Learning to Evaluate and manage ANtenatal Blood pressure at Home) cohort data. This cohort consisted of 52 healthy primigravida singleton women age 21-44 years not receiving treatment for hypertension. SBP (systolic blood pressure) and DBP (diastolic blood pressure) was obtained during hospital antenatal visits and regularly at home via patient self-monitoring using a Microlife WatchBP Home Monitor. The home vs hospital SBP and DBP was investigated to identify cases of white coat or masked hypertension. The effect of increased SBP or DBP on pregnancy outcome was analysed.
**Results:**
Results demonstrated mean hospital $(122+/-15 \ p=0.001)$ systolic blood pressure is significantly higher than home $(108+/-8 \ p=0.001)$. Moreover, hospital $(77 \pm 10 \ p=0.001)$ diastolic blood pressure is also significantly higher than home $(64 \pm 6 \ p=0.001)$.

**Discussion and Conclusion:**
Home BP monitoring appears to be a potentially useful addition to routine antenatal care. A further large randomised controlled trial is necessary and planned to identify potential statistical significance.

**Notes:**