

Proceedings of

# ACBI 2016

# 39<sup>TH</sup> Annual Conference

*Association of Clinical Biochemists in Ireland*

Radisson Blu  
Hotel & Spa, Cork



Friday & Saturday,  
November 11th & 12th

# 2016



ISSN: 1649-7651



Proceedings of  
**39<sup>TH</sup> Annual Conference**  
Association of Clinical Biochemists in Ireland

**Radisson Blu Hotel & Spa  
Cork**

November 11th & 12th, 2016



Contents

	PAGE
Message from the President .....	3
Welcome Address .....	4
Continuing Education .....	5
Acknowledgements .....	6
Conference Programme .....	8
Session 1 – Friday Morning .....	11
Session 2 – Friday Afternoon .....	15
Session 3 – Saturday .....	21
Session 4 – Saturday .....	25
Poster Index .....	28

## A message from the President of the ACBI

**Professor Maria Fitzgibbon**  
**President, ACBI**



I have great pleasure in welcoming you all, particularly our speakers, to the 39th Annual Conference of the Association of Clinical Biochemists in Ireland (ACBI). The 2016 conference is being held in Cork, some believe the true capital of Ireland!

As is tradition, the ACBI conference brings together national and international experts to present and stimulate debate in many topics in clinical laboratory medicine as well as looking to future developments. This year's programme addresses aspects of cardiovascular disease diagnosis, prognosis and research and a further theme focuses on the important and expanding area of biochemical molecular developments. The patient is central to the conference agenda with both access to, and impact of, biochemical results being presented.

Trainee clinical biochemists will present cases and controversies and robust audience participation is expected and encouraged.

Clinical Biochemistry comprises pathways, proteins, hormones, enzymes, genes, all of which have the potential to play a role in disease development, adding to the complexity of getting good diagnostic medicine for our patients. We have world-class universities in Ireland and we need to attract the best scientists, inspire and train them in clinical diagnostics. The ACBI have made good progress in attracting and developing training programmes for young graduates in the past year.

The challenge is to develop a competitive, co-dependent collaborative environment where the only aim is better clinical science, research and diagnostics. Many new technological advancements including mass spectrometry, next-generation sequencing, proteomics etc. are bound to create a bright future for scientific developments and timely improvements in diagnostics.

I look forward to our conference and I have no doubt that we will all enjoy an inspiring academic, as well as a lively social programme.

*The Quad, University College Cork*



## Welcome to ACBI 2016

On behalf of the organising committee, I am delighted to welcome you to the 39th annual conference of the Association of clinical biochemists in Ireland (ACBI)

I am pleased to welcome you to Cork for the first time since 2004. A particular word of welcome to our invited speakers and of course our corporate sponsors without whose support the conference could not be held. Their generous support is vital to ensuring the continued success of the ACBI's annual conference

The scientific programme covers new developments in cardiovascular disease, cystic fibrosis and new exciting opportunities in molecular genetics. I hope we will be challenged to think about how laboratory testing impacts on patient outcomes and whether current approaches to accreditation do indeed contribute to better quality service.

We will have time to discuss the role of ACBI in the National cancer control programmes. We will have awards for best scientific poster and clinical case presentation.

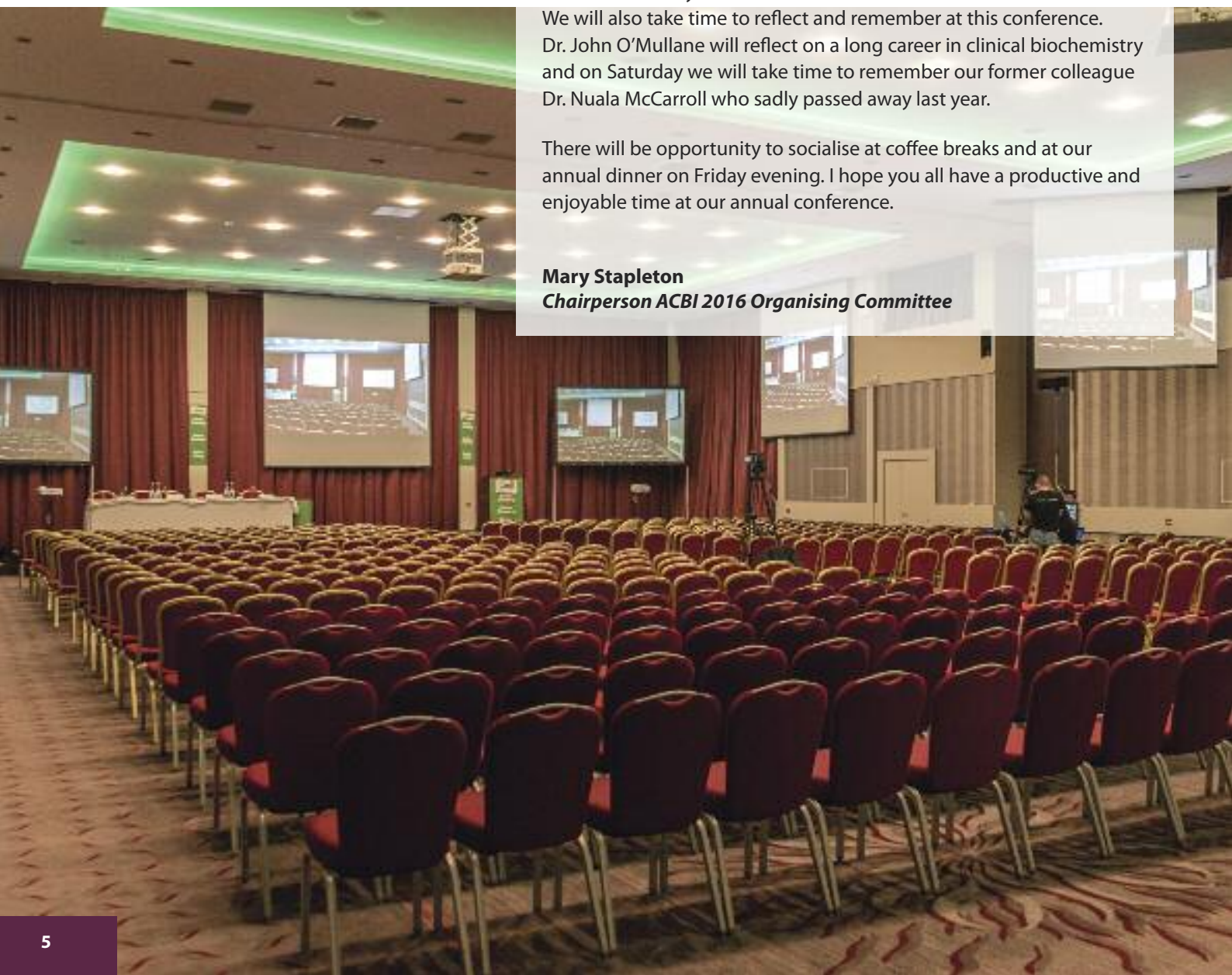
2016 has been a year of reflection and remembrance in Ireland.

We will also take time to reflect and remember at this conference. Dr. John O'Mullane will reflect on a long career in clinical biochemistry and on Saturday we will take time to remember our former colleague Dr. Nuala McCarroll who sadly passed away last year.

There will be opportunity to socialise at coffee breaks and at our annual dinner on Friday evening. I hope you all have a productive and enjoyable time at our annual conference.

**Mary Stapleton**  
**Chairperson ACBI 2016 Organising Committee**

Conference Room, Radisson Blu



## ***Royal College of Pathologists***

ACBI 2016 Conference has been approved for 9 CPD credits by the Royal College of Pathologists.

Medical staff and clinical scientists in career grade posts who are enrolled with one of the Royal Colleges for CPD purposes and attend the meeting will be entitled to receive CPD credits.

## ***Academy of Clinical Science and Laboratory Medicine***

This meeting is accredited with 5 CPD credits for attendance on Friday and 4 credits for attendance on Saturday

## ***ACBI CPD Scheme***

The ACBI CPD scheme awards one credit per hour for attendance at conferences.

The facility to collate your personal CPD is available on the member's area of the ACBI website.

*Gargoyle, St. Fin Barre's Cathedral*

**Please fill out the appropriate form on each day of your attendance. You will receive a certificate of attendance from the conference organising committee.**

## ***Evaluation of ACBI 2016***

All conference participants are requested to complete the conference evaluation form located in the delegate bag. This form is to be completed and returned to registration desk.

The Organising Committee for ACBI 2016 gratefully acknowledge the very generous support of the following:

## Major Sponsors



## Associate Sponsors



## Additional Sponsorship



ScheBo® • Biotech



ACBI 2016 was jointly organised by members from

Cork University Hospital  
and  
Mater Misericordiae University Hospital  
and  
Galway University Hospital

**Cork University Hospital**  
**Chairman:** Ms. Mary Stapleton  
Ms. Caroline Joyce  
Ms. Kelly McCarthy

**Mater Misericordiae University Hospital**  
**Dr. Maria Fitzgibbon**  
**Dr. Graham Lee**

**Galway University Hospital**  
**Dr. Paula O'Shea**



Thanks also to:

**Webmaster and Conference Coordinator:** Dermot Deverell  
**Conference Photographer:** Peadar McGing  
**Audiovisual:** AVC  
**Radisson Blu Hotel:** Aileen O'Flynn, Eithne Tighe

**Artwork/Design:** Focus Design Limited  
**Print:** Casimir Printing Limited

## Conference Opening

- 09.00 Registration and Coffee
- 10.15-10.30 **Opening Remarks – Prof. Maria Fitzgibbon, ACBI President**
- 10.30-11.00 Official Opening of ACBI Conference

## Session 1: Friday Morning

- Chair:** **Dr. Damian Griffin,**  
Consultant Chemical Pathologist, GUH
- 11.00-11.30 **Dr. Maurice O’Kane,**  
Consultant Chemical Pathologist, Altnagelvin Hospital, Derry  
***Direct Access to Patient Results***
- 11.30-12.00 **Professor Cathy Shanahan,**  
Professor of Cellular Signalling,  
Cardiovascular Division, Kings College, London  
***Vascular Calcification in CKD: Cause and Effect***
- 12.00-12.30 **Dr. Dermot Neely,**  
Consultant Chemical Pathologist,  
Royal Victoria Infirmary, Newcastle upon Tyne  
***Lipids and CVD***
- 12:30 Lunch and attended Poster Session



## Session 2: Friday Afternoon

- Chair:** **Ms. Caroline Joyce,**  
Principal Clinical Biochemist, CUH
- 14.00-14.30 **Dr. Amy Jayne McKnight,**  
Senior Lecture, School of Medicine,  
Dentistry and Biomedical Sciences, Queen’s University Belfast  
***Potential, Reality and Promise of the 100K Human Genome Project***
- 14.30-15.00 **Dr. Jillian Casey,**  
Genomic Medicine Limited  
***The Topsy-Turvy world of NGS***
- 15.00-15.30 Coffee and attended poster  
Session - sponsored by Medical Supply Company
- 15.30-16.00 **Professor Barry Plant,**  
Consultant Respiratory physician, CUH  
***CFTR Modulation in Cystic Fibrosis – an Irish Perspective***
- 16.00-16.30 **Dr. Patrick Harrison,**  
Department of Physiology, UCC  
***Development of Gene Editing as a Therapeutic Approach for Rare Diseases***
- 16.30-17.15 **Dr. John O’Mullane,**  
Consultant Clinical Biochemist, CUH  
***Reflections on an Incredible Sojourn in Biochemistry 1968-2016  
and perhaps onwards!!***



## Friday Evening

- 19.00 Drinks Reception - sponsored by Brennan & Co.
- 20.00 **Annual Dinner**



## Saturday

- 8.30-9.30 **ACBI AGM** (Ordinary members only)

## Session 3: Saturday Morning

- Chair:** **Dr. Jennifer Brady,**  
Principal Clinical Biochemist, MMUH
- 9.45-10.15 **Dr. Phillip Monaghan,**  
Consultant Clinical Biochemist,  
The Christie NHS Foundation Trust, Manchester  
***Impact of laboratory tests on patient outcomes***
- 10.15-10.45 **Prof. John Seddon,**  
Managing Director, Vanguard Consulting, UK  
***Has ISO15189 anything to do with quality?***
- 10.45-11.15 **Dr. Edmund Lamb,**  
Consultant Clinical Scientist,  
Kent and Canterbury Hospital, Canterbury  
***Biological variation and kidney function***
- 11.15-11.45 Coffee



## Session 4: Saturday

- Chair:** **Prof. Maria Fitzgibbon,**  
Consultant Clinical Biochemist, MMUH
- 11.45-12.15 **Reports from NCCP projects:**  
***Harmonisation of PSA, HCG and CA125***
- 12.15-13.00 **Session Moderator: Dr. Graham Lee,**  
Consultant Clinical Biochemist,  
Mater University/Mullingar Regional hospitals  
***Reflex, Reflective Testing and Incidental Findings: Discussion of Clinical Scenarios***
- 13.00-13.15 **Tribute to Dr. Nuala McCarroll**
- 13.15-13.30 **Awards for Best Poster and Clinical Case**
- 13.30 Conference Close followed by Lunch





What's causing it  
**will it get worse**  
*is my diagnosis correct*  
**am I sick** is he suffering a heart attack  
which woman is  
at highest risk of  
cervical cancer  
**how can I reduce**  
my post-operative  
hospitalisation costs  
**is something**  
wrong with me  
do I have cancer  
am I at risk  
what diseases  
**do I have**  
who should  
manage  
her heart disease  
who is the best candidate  
for treatment  
**how** can we predict  
and prevent disease  
is my baby in danger  
did my pap miss  
something  
is he HIV+  
will this patient  
recover quickly  
after surgery  
**is my baby**  
**healthy**  
is my treatment  
working  
**can I**  
still get  
pregnant

*I know I*  
am not at risk  
*we caught it early*  
**I know I am ok**  
*I know the treatment*  
**will work**  
I am in control  
my baby is  
fine

**I KNOW WE ARE  
SAVING LIVES**

**THE POWER OF KNOWING**

Roche Diagnostics gives you  
The Power of Knowing that you're  
using accurate information to  
make the right decisions today,  
so your patients can experience  
a healthier tomorrow.



## Session 1

Roche

**Chair:**

**Dr. Damian Griffin**

Consultant Chemical Pathologist, GUH

**Dr. Maurice O'Kane**

Consultant Chemical Pathologist,  
Altnagelvin Hospital, Derry

**Direct Access to Patient Results**

**Professor Cathy Shanahan**

Professor of Cellular Signalling,  
Cardiovascular Division, Kings College, London

**Vascular Calcification in CKD: Cause and Effect**

**Dr. Dermot Neely**

Consultant Chemical Pathologist,  
Royal Victoria Infirmary, Newcastle upon Tyne

**Lipids and CVD**

*St. Fin Barre's Cathedral,  
Cork*

## Session 1

**Dr. Maurice O'Kane**  
**Consultant Chemical Pathologist,**  
**Altnagelvin Hospital,**  
**Derry.**



### **BIOGRAPHY**

*Dr O'Kane graduated in Medicine at the University of Edinburgh and undertook postgraduate training in Scotland, N. Ireland and France. He has been*

*a consultant chemical pathologist at Altnagelvin Hospital, Derry since 2016.*

*His major clinical interests are point-of-care testing, familial hypercholesterolaemia and diabetes mellitus. Other professional activities include Director of Clinical Practice at the Association for Clinical Biochemistry and Laboratory Medicine [ACB], associate editor of the Annals of Clinical Biochemistry.*

*From 2007 – 2016 Dr O'Kane was Director of Research at the Western Health and Social Care Trust and chief executive officer of the Clinical Translational Research and Innovation Centre [C-TRIC]. He is currently the Director of the N. Ireland Clinical Research Network and chairs the Steering Committee of the N. Ireland Biobank.*

### ***Direct Patient Access to Test Results***

The last three decades have seen a major change in the culture of healthcare delivery with patients now at the centre of all clinical decision making. This has resulted in greater patient engagement, greater satisfaction with care and increased transparency in the delivery of care. An important element has been patient access to medical records which is now enshrined in law in several countries.

Since April 2015 all GP practices in England are required to give patients online access to a summary of their medical history. In 2014 the US Department of Health and Human services requires all laboratories to make test results available to patients within 30 days of receipt of a request. There is abundant evidence that many patients strongly welcome direct access to test results. This might allow greater patient engagement with care, especially in the self-management of chronic disease and also act as an additional safety net if clinically important results e.g. cancer diagnosis are overlooked by clinical staff. Concern has been expressed that direct patient access might cause anxiety for patients and might increase the workload of clinical staff. There is only limited evidence to support these concerns.

Direct patient access to test results will have significant implications for laboratories, in particular there may be a need to develop alternative ways of presenting test results to facilitate greater patient understanding. The conventional approach of reporting a numerical result with a healthy population reference range appears not to be universally understood by patients. There is a need for research on how laboratories can best present test results and engage with patients in a way that contributes best to safe and effective care.

## Session 1

### Vascular Calcification in Chronic Kidney Disease: Cause and Effect

Vascular calcification is a ubiquitous feature in the ageing population and is accelerated in patients with chronic kidney disease (CKD) where it is associated with increased mortality, morbidity and surgical intervention. It occurs at two anatomical sites in the vessel wall; the intima in association with atherosclerosis and the media, most prevalent in CKD and ageing. These calcifications were once considered to be due to passive degenerative processes however, accumulating evidence suggests that calcification is driven by cell-mediated processes similar to bone formation. A number of VSMC-mediated processes are required for calcification to occur: Firstly, VSMCs can undergo osteo/chondrocytic differentiation. This is characterized by upregulation of a number of mineralization-regulating proteins and ECM components normally expressed in bone<sup>1</sup>. The most important of these is the master bone regulatory transcription factor (TF) Runx2 which activates its putative targets alkaline phosphatase (ALP), bone sialoprotein (BSP) and osteocalcin (OCN). Other key events in the induction of calcification are loss of expression/function of local (Matrix Gla protein (MGP)) and circulating (fetuin-A) inhibitors of calcification<sup>2</sup>. In addition, apoptosis<sup>3</sup> as well as membrane bound vesicles released from phenotypically modified VSMCs have an essential role in promoting calcification by forming the first nidus for mineralization. Studies focussing on the specific factors that induce a 'calcific milieu' in patients as well as factors that may be targeted for intervention such as (1) increasing inhibitor function and (2) blocking maladaptive signalling that promotes osteogenic differentiation, are now key to ameliorating this disease process.

The physiological environment in patients with CKD and particularly those on dialysis is exceedingly 'pro-calcific'. Dysregulated mineral metabolism resulting in chronically high circulating levels of phosphate as well as transient bouts of hypercalcemia potentially induce VSMCs to undergo specific phenotypic changes that promote calcification<sup>4,5</sup>. These defects in mineral metabolism are also exacerbated by dysregulated bone metabolism that potentially acts to drive further vascular mineralization. Importantly, emerging evidence suggests that calcification is an indicator of a 'prematurely aged' vasculature and that dysregulated mineral metabolism may be a key driver of accelerated ageing<sup>6</sup>. We are currently exploring this idea using in vitro and ex vivo models of vascular calcification.

**Professor Cathy Shanahan**  
**Professor of Cellular Signalling,**  
**Cardiovascular Division,**  
**Kings College, London**



#### BIOGRAPHY

Professor Cathy Shanahan obtained her BSc(Hons) and PhD in Genetics from the University of Adelaide, Australia. She worked for CSIRO in Sydney, Australia before moving to the

University of Cambridge as a post-doc in the Departments of Biochemistry and then Medicine.

In 1995 she was appointed as a British Heart Foundation Basic Sciences Lecturer and in 2005 became a British Heart Foundation Senior Fellow in the Department of Medicine, University of Cambridge. In 2007 she took up the position of Professor of Cellular Signalling at King's College London. Her work focuses on mechanisms of vascular smooth muscle cell (VSMC) dysfunction in ageing and disease.

<sup>1</sup> Iyemere VP, Proudfoot D, Weissberg PL and Shanahan CM. Vascular smooth muscle cell phenotypic plasticity and the regulation of vascular calcification. *J Intern Med*. 2006;260:192-210.

<sup>2</sup> Kapustin AN and Shanahan CM. Calcium regulation of vascular smooth muscle cell-derived matrix vesicles. *Trends Cardiovasc Med*. 2012;22:133-7.

<sup>3</sup> Shroff RC, McNair R, Figg N, Skepper JN, Schurgers L, Gupta A, Hiorns M, Donald AE, Deanfield J, Rees L and Shanahan CM. Dialysis accelerates medial vascular calcification in part by triggering smooth muscle cell apoptosis. *Circulation*. 2008;118:1748-57.

<sup>4</sup> Shanahan CM, Crouthamel MH, Kapustin A and Giachelli CM. Arterial calcification in chronic kidney disease: key roles for calcium and phosphate. *Circ Res*. 2011;109:697-711.

<sup>5</sup> Kapustin AN, Chatrou ML, Drozdov I, Zheng Y, Davidson SM, Soong D, Furmanik M, Sanchis P, De Rosales RT, Alvarez-Hernandez D, Shroff R, Yin X, Muller K, Skepper JN, Mayr M, Reutelingsperger CP, Chester A, Bertazzo S, Schurgers LJ and Shanahan CM. Vascular smooth muscle cell calcification is mediated by regulated exosome secretion. *Circ Res*. 2015;116:1312-23.

<sup>6</sup> Shanahan CM. Mechanisms of vascular calcification in CKD-evidence for premature ageing? *Nat Rev Nephrol*. 2013;9:661-70.

## Session 1

**Dr R Dermot G Neely**  
**BSc MD FRCP FRCPath**  
**Consultant Chemical Pathologist,**  
**Royal Victoria Infirmary, Newcastle**  
**upon Tyne**



### **BIOGRAPHY**

*Dermot Neely is a Consultant in Clinical Biochemistry and Metabolic Medicine and former Clinical Director of Laboratory Medicine, Newcastle upon Tyne Hospitals NHS Trust.*

*He is presently Head of the Newcastle Lipid Clinic based at the Royal Victoria Infirmary, Chairman of the Lipid Specialists Advisory Group of the North Clinical Networks and Clinical Lead for the Regional FH Genetic Cascade Testing Programme, launched in 2014. He is also Director of the Newcastle Supra-Regional Assay Service Cardiovascular Biomarkers and Endocrine Laboratories and a member of the executive group of the Newcastle NIHR Diagnostic Evidence Co-operative.*

*As a member of the NICE Lipid Modification Clinical Guideline (GC181) Development Group and NICE Diagnostics Advisory Committee he is committed to the implementation of evidence based clinical and laboratory practice. His major research interests are in cardiovascular biomarkers and genetic dyslipidaemias including FH. An Honorary Clinical Lecturer at the University of Newcastle upon Tyne he also teaches on cholesterol, lipids and related aspects of metabolic medicine in the undergraduate medical curriculum. He is a member of the editorial boards of Atherosclerosis and British Journal of Cardiology.*

*Dr Neely is a founder Trustee of the HEART UK, the Cholesterol Charity and co-Chairman of the HEART UK Familial Hypercholesterolaemia Intelligence Network (FHIN).*

### ***Lipids and CVD***

The causative role of plasma lipids and lipoproteins in combination with other risk factors, in the development of cardiovascular disease has been demonstrated in large prospective and case-control studies. These findings have been reinforced by studies of genetic variants associated with increased plasma lipids and lipoproteins which also increase CVD risk and by large clinical outcomes studies of cholesterol lowering treatment which have proven that reduction of plasma lipids is effective in reduction of cardiovascular morbidity and mortality. Plasma lipid profiles are abnormal in over 70% of patients with premature cardiovascular disease and are found to be familial dyslipidaemias in more half of cases. Despite the wealth of evidence only a minority of those who would benefit are offered effective lipid modifying therapy. The achievement of better outcomes will require much earlier diagnosis of genetic lipid disorders and the prompt recognition of common dyslipidaemias associated with unhealthy diet and lifestyle. The clinical laboratory can help improve access to plasma lipid and lipoprotein tests by recommending routine use of non-fasting samples, supported by links to clear, evidence based guidelines for interpretation, management and further investigation as required.

## Session 2



### Chair:

**Ms Caroline Joyce**, Principal Clinical Biochemist, CUH

### **Dr. Amy Jayne McKnight**

Senior Lecture, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast

### **Potential, Reality and Promise of the 100K Human Genome Project**

**Dr. Jillian Casey**, Genomic Medicine Ireland Ltd.

### **The Topsy-Turvy world of NGS**

### **Professor Barry Plant**

Consultant Respiratory physician, CUH

### **CFTR Modulation in Cystic Fibrosis – an Irish Perspective**

**Dr. Patrick Harrison**, Department of Physiology, UCC

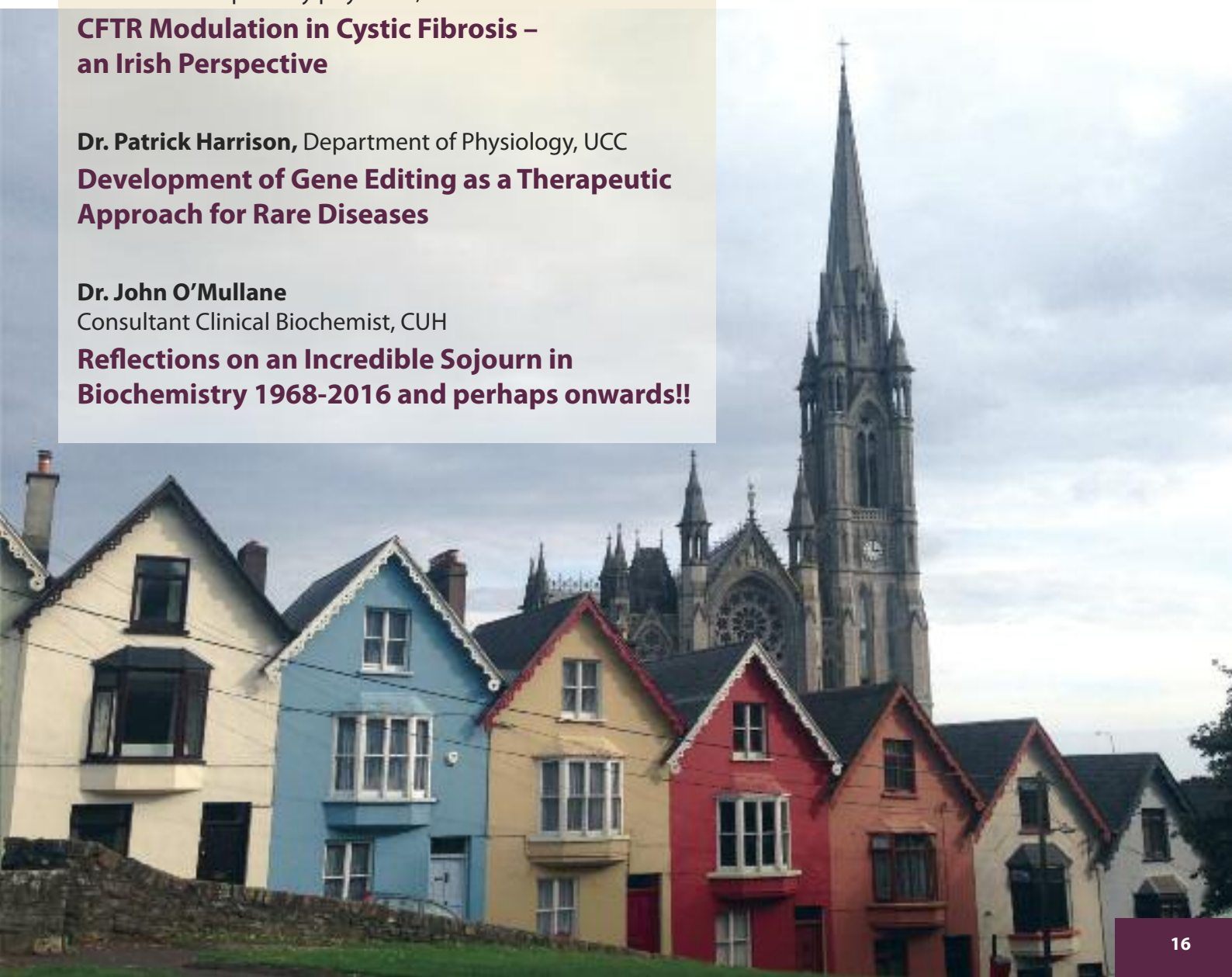
### **Development of Gene Editing as a Therapeutic Approach for Rare Diseases**

### **Dr. John O'Mullane**

Consultant Clinical Biochemist, CUH

### **Reflections on an Incredible Sojourn in Biochemistry 1968-2016 and perhaps onwards!!**

*Cobh, Co. Cork*



## Session 2

**Dr. Amy Jayne McKnight**  
*Senior Lecture, School of Medicine,  
Dentistry and Biomedical Sciences,  
Queen's University Belfast*



### BIOGRAPHY

*Dr Amy Jayne McKnight's genomic research team primarily use state-of-the-art tools to identify genomic risk factors for human diseases, and investigate how*

*each person's genes interact with their environment.*

*As senior lecturer at Queen's University of Belfast AJ has published >85 original research papers. She is the rare disease research lead for the recently funded NI Genomic Medicine Centre contributing to 100 KGP, a director of the NI Rare Disease Partnership, helped develop the NI rare disease strategy, and is part of the Northern Ireland Rare Disease Implementation group*

### ***Potential, reality, and promise of 100 KGP***

Rapid technological and analytical advances have led to significant increases in the amount of genomic data being generated and evaluated for multiple traits. These developments offer significant potential to improve disease prediction, diagnosis, prognosis, and provide insights for underlying disease mechanisms, however the route has not been as easy as first anticipated. Nonetheless, the 'genomics revolution' has led to multiple early successes with improved diagnosis and optimised treatment strategies for rare diseases in particular.

The 100,000 genomes project (100 KGP) was launched as a transformational scheme to create a new genomic medicine service within the NHS, UK. Discussing Northern Ireland's rare disease developments and our participation in 100 KGP will provide a brief overview of 100 KGP, including logistical considerations such as clinical-genomic correlations, ethics and governance. The potential and practical reality of delivering diagnosis, enabling medical research, building local capacity and skills in next generation sequencing with associated bioinformatics, and leaving a lasting legacy are important considerations.

The 100 KGP represents a tremendous opportunity to work with patients, scientists, healthcare professionals, and other stakeholders to create a databank of detailed genomic information correlated to electronic medical records that may be federated with colleagues worldwide.

## Session 2

### *The topsy-turvy world of NGS*

Next Generation Sequencing (NGS) has fast become a front line genetics tool for identifying the molecular basis of inherited disorders. The ability to sequence thousands of genes in one test offers an attractive alternative to single gene testing, particularly for rare or complex disorders. Through our own research, we see how NGS is helping patients and families to obtain long-awaited diagnoses. Therefore, it is not surprising that this new tool has started to transition from the research laboratory into clinic.

However, through our research, we have identified challenges and pitfalls that can complicate analysis and interpretation of NGS including (i) variants of unknown significance, (ii) atypical phenotypes, and (iii) phenotypic variability – clinical heterogeneity or more than one recessive disorder?

Proving that exome findings are indeed causal can also be challenging. How much evidence is required for an exome finding to become a diagnosis? We have encountered a number of issues that impede diagnosis including (i) DNA samples unavailable for segregation analysis, (ii) only partial clinical/histopathological overlap with newly-described syndromes and (iii) questionable pathogenicity of published findings. The timeline for clinical validation of a research finding can also be lengthy, particularly for rare or novel disease genes where pathogenicity is difficult to interpret.

Our experience is that NGS can be of significant benefit in the clinic. However, our findings also show a need for caution when it comes to data interpretation; a cavalier approach could result in misdiagnoses.

**Dr. Jillian Casey**  
**Genomic Medicine Ireland Ltd.**



#### **BIOGRAPHY**

*Dr Jillian Casey is a Consultant with Genomics Medicine Ireland, a life-sciences company researching the relationship between genetics and disease.*

*Previously, she worked as a Research Associate at Temple Street Children's University Hospital, the National Children's Research Centre and the UCD Academic Centre on Rare Diseases. She was awarded her PhD in Medical Genetics from University College Dublin where her research studies focused on the molecular pathogenesis of rare inherited disorders.*

*Dr Casey works closely with clinicians to characterise undiagnosed paediatric disorders using next-generation sequencing approaches. Her recent studies have focused on developmental delay syndromes. She believes that identifying the genetic causes of rare disorders in the Irish population is the first step in translating basic health research to the bedside. As a result of her studies, new disease genes for a range of paediatric disorders have been identified and translated into the diagnostic clinic to facilitate early diagnosis and intervention.*

## Session 2

### Professor Barry Plant

MB, BMedSc, MD, FRCPI

**Consultant Respiratory Physician  
(CUH) and Professor, Dept. of  
Medicine (UCC)**

### ***CFTR Modulation in Cystic Fibrosis – an Irish Perspective***



#### **BIOGRAPHY**

*Barry Plant is a  
Consultant  
Respiratory  
Physician, Director  
of the Adult Cystic  
Fibrosis Centre in  
Cork University  
Hospital and Senior  
Clinical Lecturer at*

*University College Cork. He was awarded MB  
MCH MAO BMedSc degrees from UCC and an  
MD from UCD. His research interests include  
innate immune responses in cystic fibrosis (CF),  
microbiota in CF, aging in CF, emerging  
therapies for lung diseases and non-invasive  
diagnostic imaging.*

*Professor Plant is extensively published in  
international medical journals (including  
NEJM, Lancet Respir Med, Thorax, Chest, ERJ  
and AJRCCM) and textbooks in all areas of  
lung disease. He has been an invited speaker  
by many international societies including the  
American Thoracic Society, the Irish Thoracic  
Society, the European Respiratory Society, the  
Australasian CF Society, the European CF  
Society and the Food and Drug Administration  
USA.*

## Session 2

### *The Z to A of Gene Editing as a Therapeutic Approach for Rare Diseases*

Gene editing offers the potential to precisely edit the DNA sequence in the genome of every cell in an organism. Over the last 11 years, the technique has completely changed our ability to manipulate the mammalian genome in experimental animals, and now looks set to radicalise the therapeutic approach for rare diseases – if DNA mutations cause disease, then let gene editing correct them.

But is it really that simple? Our lab has corrected life-threatening Cystic Fibrosis mutations in isolated cells, many other labs have corrected hundreds of other disease-causing mutations in similar model systems, but what about clinical application – surely that's decades into the future? No, gene edited cells have already transformed the lives of at least two patients, eradicating HIV from one, and eradicating lymphoma from another.

In my talk, I will describe the steps our lab are taking to progress gene editing for CF, and highlight other examples from other diseases that are almost ready for clinical trials. I will discuss mechanisms of precision gene editing, alternative approaches to excise deleterious DNA sequences, show how gene editing can be used to modify the genome without even cutting the genome, and explain the pros and cons of the full range of gene editing tools from ZFNs, TALENs and Cas9 (the CRISPR you've heard of), to AsCpf1 (the CRISPR you've not).

#### Recent Publications

- Analysis of gene repair tracts from Cas9/gRNA double-stranded breaks in the human CFTR gene Hollywood JA et al. (2016) Scientific Reports 6: 32230.
- Impact of gene editing on the study of cystic fibrosis. Harrison PT et al. (2016) Hum Genet. 135(9):983-92.
- Genetic medicines for CF: Hype versus reality. Alton EW et al. (2016) Pediatr Pulmonol. 51(S44):S5-S17.

**Patrick Harrison PhD**  
**Senior Lecturer**  
**BioSciences Institute/Department**  
**of Physiology**  
**University College Cork**



#### BIOGRAPHY

*The focus of Dr Harrison's lab is the development gene editing for treatment of rare diseases. His early work in this field pioneered the use of ZFNs and CRISPR to*

*successfully repair the most common CF-causing mutation, F508del, in cell culture. The current focus extends the work to correct CF mutations of the deep intron theratype in primary cells, stem cells and animal models. Dr. Harrison is a principal investigator in the CF Trust's Gene Editing Strategic Research Centre, and has additional grant funding from the CF Foundation (USA), with collaborations across Europe and the US. He is also using CIRSPR editing to model metabolic disorders such as the lysosomal storage disorder Cystinosis, a collaborative project funded by the HRB and Cystinosis Ireland, and is developing editing for skin disorders such as atopic dermatitis and Epidermolysis Bullosa.*

## Session 2

### Dr. John O'Mullane

**BSc., MSc., PhD., FRC Path., Dip.CB.,  
EuSpLM**

**Consultant Clinical Biochemist, CUH**



#### **BIOGRAPHY**

*John O'Mullane was Consultant and Senior Clinical Lecturer in Clinical Biochemistry at CUH/UCC, a post he had held since 1999 up to his retirement in September 2016. He is a Fellow of the Royal College of Pathologists*

*and spent over forty years in the practice of clinical biochemistry in service, academic, research and professional capacities. His recent professional roles included membership of The Irish Medical Council, The Advisory Committee on Medical Devices (IVDD) of the Irish Health Products Regulatory Authority. He is the Irish National Member to the European Committee for Clinical Chemistry and Laboratory Medicine's Higher Specialist Register. He is a registered Clinical Scientist with Health Care Professions Council (HCPC) UK and is a current Council Member of CORU. He is also a fully trained Peer Assessor for UKAS / CPA Clinical Pathology Accreditation UK.*

*He represented Laboratory Medicine sitting on the Higgins Reconfiguration Forum for The Health Services in Cork and Kerry as the Clinical Director for Laboratory Medicine. This work informed the Hospital Group Structures.*

*He was Senior Lecturer in Biomedical Sciences prior to his current appointment, taking a lead role in the development of the joint undergraduate and post graduate programmes in Biomedical Sciences at University College Cork and Cork Institute of Technology. His academic teaching roles included contributions to Medical, Nursing and Scientific third level undergraduate and post graduate programmes at UCC, TCD DCU and DIT.*

*Dr. O' Mullane was President, Vice President and uniquely has held all Council office positions of the ACBI. His research interests include analytical clinical biochemistry, laboratory diagnostics and biochemistry education with peer review publications in each of these areas. He has supervised many pursuing masters, doctoral and post-doctoral studies. His service commitment over four decades included practice in all clinical biochemist grades of practice covering periods in Dublin at St Vincent's, St James's, Crumlin, Temple St. hospitals Our Lady of Lourdes in Drogheda, Galway University Hospital and finally at Cork University Hospital.*

### ***Reflections on an Incredible Sojourn in Biochemistry 1968-2016 and perhaps onwards!!***

A personal series of reflections about a career in clinical biochemistry spanning over four decades of practice in the Irish Public Health Services and the associated University / Institute of Technology Education Services.

The emphasis chosen will be based on my journey and observations from the late sixties to the present time. It may not accord with colleagues' views and opinions. Indeed some of the narrative may well have taken place before some present were born. It will be somewhat self-indulgent for which I will take full and sole responsibility. Some views on "whither now" may be exceedingly speculative as the rate of change, paradoxically the only constant, continues to confound.

## Session 3



### Chair:

**Dr. Jennifer Brady**

Principal Clinical Biochemist, MMUH

**Dr. Phillip Monaghan**

Consultant Clinical Biochemist,  
The Christie NHS Foundation Trust, Manchester

**Impact of laboratory tests on patient outcomes**

**Prof. John Seddon**

Managing Director, Vanguard Consulting, UK

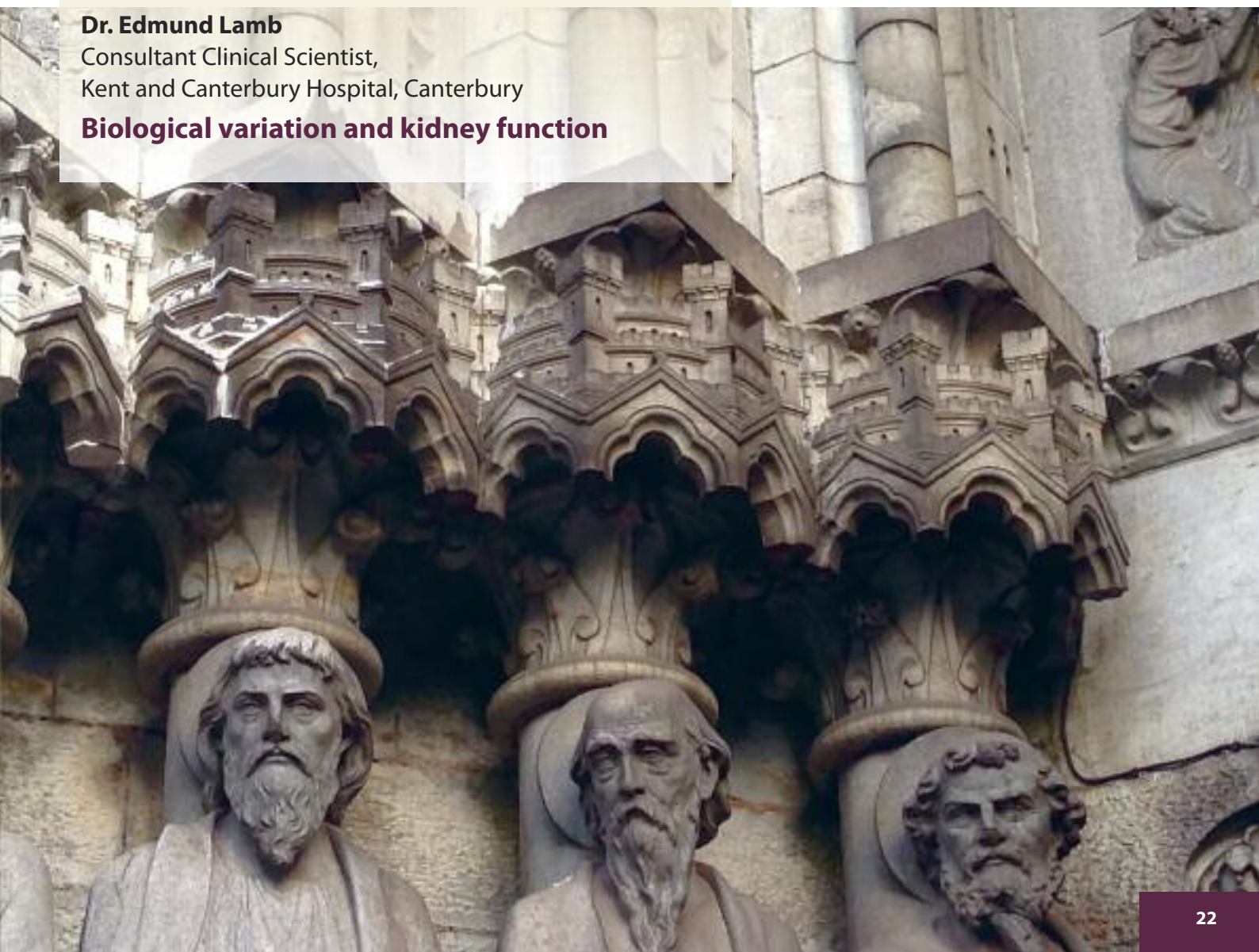
**Has ISO15189 anything to do with quality?**

*Detail - St. Fin Barre's Cathedral*

**Dr. Edmund Lamb**

Consultant Clinical Scientist,  
Kent and Canterbury Hospital, Canterbury

**Biological variation and kidney function**



## Session 3

### **Dr. Phillip Monaghan** **Consultant Clinical Scientist** **The Christie Pathology Partnership**



#### **BIOGRAPHY**

*After graduating from the University of Manchester Institute of Science and Technology (UMIST) in Biochemistry with Applied Molecular Biology, I went on to complete my PhD in*

*Protein Biochemistry at the University of Leicester. I subsequently commenced my training in Clinical Biochemistry at Wirral University Teaching Hospital, Alder Hey Hospital and University Hospital of South Manchester. I have been a Clinical Scientist at The Christie NHS Hospital for over 6 years, obtaining Fellowship of the Royal College of Pathologists (FRCPath) in 2014. I am a state registered Clinical Scientist with the Health and Care Professions Council (UK) and a European Specialist in Clinical Chemistry and Laboratory Medicine (EuSpLM).*

*I am Honorary Lecturer at the University of Manchester in the Faculty of Medical and Human Sciences, Institute of Inflammation and Repair, and regularly teach on the MSc Clinical Sciences programme.*

*I am currently a Member of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Test Evaluation (WG-TE).*

*I am Deputy Chair of the Association for Clinical Biochemistry and Laboratory Medicine (ACB) Scientific Committee's Working Group on Traceability and Harmonisation of Calibration (WGTHC), UK.*

*Special interests include evidence-based medicine (test evaluation), biochemical endocrinology & neuroendocrinology and assay interference studies.*

*I was awarded the Silver Research Medal from the Royal College of Pathologists in 2012 for my work on serum cortisol measurement in Cushing's disease. More recently, I was a Finalist at the 2016 Chief Scientific Officer's Healthcare Science Awards.*

*To date, I have published 20 scientific papers in international peer-reviewed journals.*

### ***Impact of Laboratory Tests on Patient Outcomes***

Almost every clinical pathway relies on patients having access to pathology services. Clinical pathways describe the interconnection of medical testing to downstream clinical management, thus providing an indirect link between testing in laboratory medicine and patient health outcomes. This presentation will highlight the central role clinical pathways play in the identification of unmet clinical needs to guide the development of new medical tests.

Unmet clinical needs drive the development of treatments, but are rarely defined and assessed when developing medical tests. In reality, new tests are often developed through technology innovations, rather than as a result of considering the 'added-value' of testing in a clinical pathway and its impact on improving patient outcomes. In the context of medical testing, unmet clinical need is defined as any missing or inadequately performing component of a clinical pathway. To evaluate if a new in vitro diagnostic (IVD) medical test is able to address a current unmet clinical need requires a full consideration of its intended use (test purpose) and positioning (test role) in the clinical pathway and how the test may contribute to the effectiveness of care delivered (outcome).

## Session 3

### *Has ISO 15189 anything to do with quality?*

ISO 15189 is promulgated as a quality standard. John Seddon argues that it is based on bad theory and can only lead to sub-optimisation of pathology services.

**Professor John Seddon**  
**Managing Director,**  
**Vanguard Consulting, UK**



#### **BIOGRAPHY**

*John Seddon has received numerous academic awards for his contribution to management science. He is the leader of the Vanguard organisations, operating in nine countries, and the originator of the Vanguard Method, the means by which service organisations change from a conventional command and control design to a systems design. John is an ardent critic of ISO standards, arguing that they impede improvement and damage morale. He is the author of 'The Case Against ISO 9000' (1997, now out of print). John's latest book (The Whitehall Effect: How Whitehall became the enemy of great public services and what we can do about it) is published by Triarchy Press.*

## Session 3

**Dr. Edmund Lamb**  
**Consultant Clinical Scientist,**  
**Kent and Canterbury Hospital,**  
**Canterbury**



### BIOGRAPHY

*Dr Edmund Lamb is a Consultant Clinical Scientist and Head of Clinical Biochemistry at East Kent Hospitals University NHS Trust. He has over 30 years experience as an NHS clinical scientist and*

*has a special interest in kidney disease.*

*His research interests relate to the use of biochemical markers to diagnose and monitor kidney disease, including the assessment of kidney function using estimated GFR and cystatin C and the evaluation of renal bone disease: he is coauthor of more than 80 peer-reviewed papers in this area. He is the chief investigator on several National Institute of Health Research RfPB and HTA funded studies investigating aspects of kidney function testing. He was a member of the Guideline Development Group on the NICE Chronic Kidney Disease Guideline (2008 and 2014) and has been involved in other national and international committees and guidelines (e.g. KDIGO CKD Guideline Development Group) including the Department of Health initiative to roll-out eGFR across England. He is Editor-in-Chief of the Annals of Clinical Biochemistry.*

### **Biological variation and kidney disease**

Renal medicine relies heavily on quantitative laboratory data for patient management, for example diagnosis and classification of chronic kidney disease (CKD) is based primarily upon measurement of serum creatinine/estimated GFR and urinary albumin. A critical issue is the ability of biomarkers to detect CKD progression: objective evaluation of the significance of serial changes in results requires knowledge of biological and analytical variation. Measured GFR itself has intrinsic variability of approximately 7%, and variability of estimated GFR is of a similar, though lesser, order.

Taking both analytical and biological variation into account, a true change in kidney function in an individual (i.e. that exceeding the reference change value, RCV) can only be inferred to have occurred when the positive/negative change in MDRD estimated eGFR exceeds 13%/15%. For example, if baseline MDRD eGFR (mL/min/1.73m<sup>2</sup>) in an individual is 50, significant increases or decreases would be to values >57 or <44 respectively. Biological variability of urinary albumin is well-researched, but often not taken into consideration in epidemiological studies: point estimates of disease prevalence will be lower when multiple measures are used. In the setting of acute kidney injury there is a need to consider biological variation data of biomarkers (e.g. urinary NGAL, KIM-1) for the purpose of disease detection, to compare markers against each other and to assess whether correction for urinary concentration is desirable.

Biological variation may differ in chronic disease states compared to health, although much available evidence relates to variation in health. Biomarkers used to monitor treatment effect in dialysis patients (e.g. haemoglobin, parathyroid hormone) have higher variance in stable dialysis patients than in healthy controls. In many of the above examples the RCVs exceed what most clinicians would consider a clinically significant change: it is likely management is being adjusted in response to changes that simply reflect biological variation. It is crucial that this message is clearly conveyed to our clinical colleagues. This talk will provide examples of application of biological variation data in nephrology.

## Session 4



**Chair: Prof. Maria Fitzgibbon**  
Consultant Clinical Biochemist, MMUH

**Session Moderator: Dr. Graham Lee**  
Consultant Clinical Biochemist,  
Mater University/Mullingar Regional hospitals

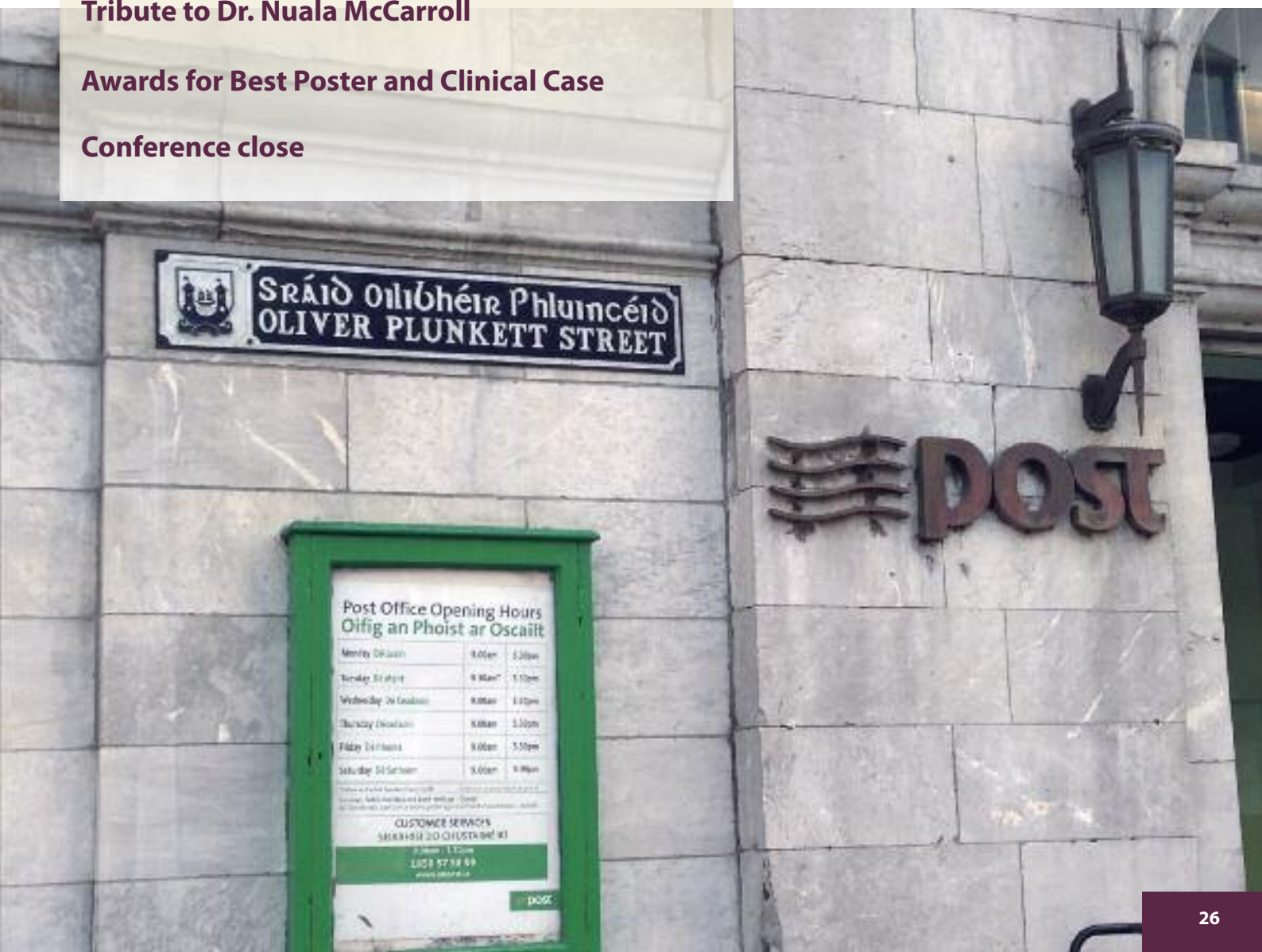
**Reflex, Reflective Testing and Incidental Findings:  
Discussion of Clinical Scenarios**

**Reports from NCCP projects:  
Harmonisation of PSA, HCG and CA125**

**Tribute to Dr. Nuala McCarroll**

**Awards for Best Poster and Clinical Case**

**Conference close**



## Session 4

### *NCCP Projects*

Members of the ACBI, in conjunction with other professional groups have been involved in a range of projects with the National Cancer Control Programme (NCCP). These include the national projects on diagnosis and management of prostatic cancer, ovarian cancer and gestational trophoblastic disease. An update on these projects will be presented.

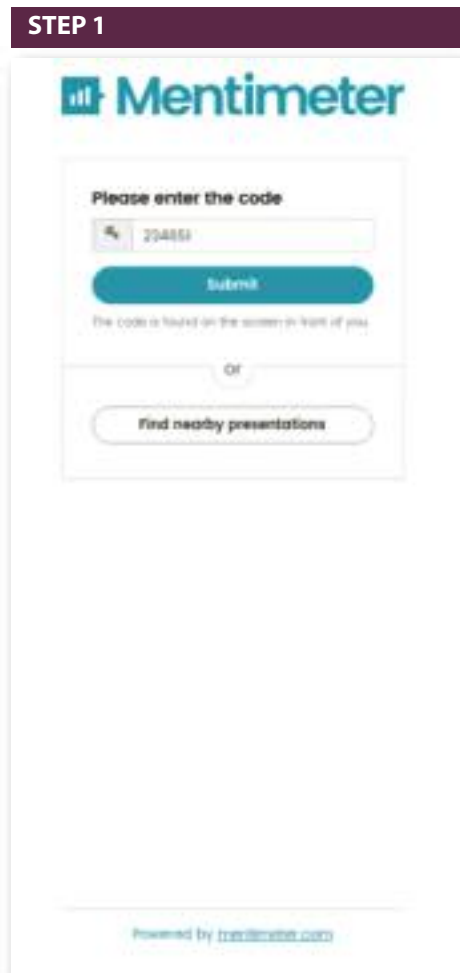
### *Reflex, Reflective Testing and Incidental Findings: Discussion of Clinical Scenarios*

This session will use clinical scenarios to introduce these important topics, pertinent to clinical and molecular biochemistry. This is an opportunity for delegates to actively participate, through discussion and real time voting using "Mentimeter"

#### **Please practice using Mentimeter (30 seconds!):**

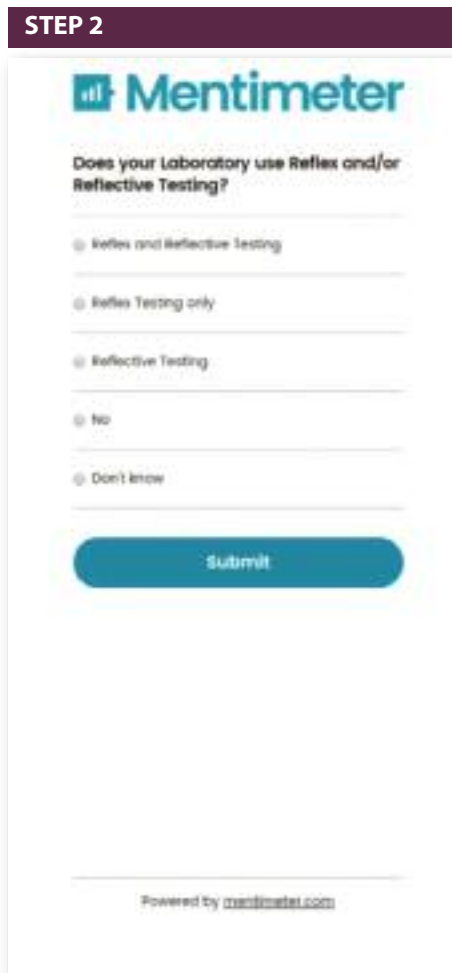
On your Laptop, Tablet or Mobile go to [www.menti.com](http://www.menti.com) and type the code 23 46 51, then "Submit". Select one of the options to the question, then select "Submit". That's all for now!

#### STEP 1



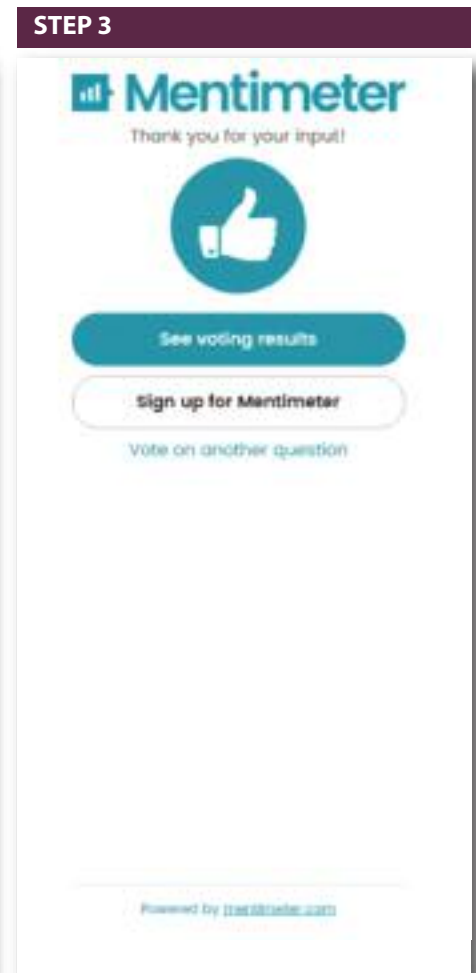
The screenshot shows the Mentimeter mobile app interface for Step 1. At the top is the Mentimeter logo. Below it, the text "Please enter the code" is displayed. There is a text input field containing the code "234651". Below the input field is a blue "Submit" button. A small note below the button says "The code is found on the screen in front of you". Below this, there is an "OR" separator and a button labeled "Find nearby presentations". At the bottom, it says "Powered by [www.menti.com](http://www.menti.com)".

#### STEP 2



The screenshot shows the Mentimeter mobile app interface for Step 2. At the top is the Mentimeter logo. Below it, the question "Does your Laboratory use Reflex and/or Reflective Testing?" is displayed. There are five radio button options: "Reflex and Reflective Testing", "Reflex Testing only", "Reflective Testing", "No", and "Don't know". At the bottom is a blue "Submit" button. At the bottom, it says "Powered by [www.menti.com](http://www.menti.com)".

#### STEP 3



The screenshot shows the Mentimeter mobile app interface for Step 3. At the top is the Mentimeter logo. Below it, the text "Thank you for your input!" is displayed. There is a large blue thumbs-up icon. Below the icon is a blue button labeled "See voting results". Below that is a button labeled "Sign up for Mentimeter". At the bottom, it says "Vote on another question". At the bottom, it says "Powered by [www.menti.com](http://www.menti.com)".



**MedLab**  
PATHOLOGY

## MedLab Pathology

### *Providing You With A First Class Pathology Testing Service*

MedLab Pathology (MLP) is accredited to the ISO 15189:2012 (296MT) medical testing standard, we offer comprehensive multi-disciplinary pathology services to GP's and hospitals throughout Ireland. MLP was established in May 2010 as Sonic Healthcare's Irish laboratory facility. MLP has been developed to bring together Sonic Healthcare's proven international capabilities and local expertise to provide internationally recognised best practice developments in laboratory medicine. We are committed to delivering service excellence through our dedicated clinical, scientific, customer service and logistics staff.

### *UK Joint Venture with NHS Hospitals*

Sonic Healthcare Limited UK subsidiary, The Doctor's Laboratory (TDL), has formed a progressive partnership, with the University College London Hospital NHS Foundation Trust (UCLH) and The Royal Free London NHS Foundation Trust (The Royal Free), called Health Service Laboratories (HSL), to provide state-of-the-art pathology and analytical services to the National Health Service (NHS). The purpose is to deliver medically-led diagnostics, innovation, value and long-term investment to healthcare.

Health Service Laboratories (HSL) flagship laboratory, the Halo, marks a significant step forward in the way pathology is conducted in the UK. Situated opposite the renowned Crick Institute, next to the Wellcome Trust and adjacent to some of the finest hospitals and medical schools in Europe, it will be transformational in the delivery of a new kind of healthcare. Currently in development, it is spread over 11 floors with five split-level basements, the facility will be home to more than 1,000 staff working within a connected suite of laboratories spanning more than 100,000 square feet. The Halo will also have dedicated clinical and non-clinical cores for vertical connectivity.

Within Halo, we have the best that science can offer, providing excellent service levels, the very best laboratory facilities for extensive research and harnessing the skills of some of the brightest minds in medicine. All working to ensure that pathology is at the heart of health, revolutionising the way we deliver an even better and more personalised standard of care.

### *Come Meet the Team*



**MLP will be at the ACBI Annual Conference this year. Why not visit us to hear more about MLP's services and what we can offer you.**



**MedLab**  
PATHOLOGY

#### **For More Information**

If you would like more information on MLP's services please contact our Sales Department on [sales@medlabpathology.ie](mailto:sales@medlabpathology.ie) or 1800 303 349



**SONIC**  
HEALTHCARE

## 1. An unusual case of Pseudohyponatraemia

Maguire, OC<sup>1</sup>, Singh, K<sup>2</sup>, Barden, E<sup>3</sup> and McCormick, PA<sup>2</sup>

<sup>1</sup>Department of Clinical Chemistry,

<sup>2</sup>Liver Unit, St Vincent's University Hospital, Dublin

<sup>3</sup>Department of Biochemistry, Mercy University Hospital, Cork

## 2. An Analysis of Factors Influencing Sample Rejection Trends for Faecal Immunochemical Testing (FIT) in the Irish National Bowel Screening Programme

Halina Antonowicz, Ethna O'Shea, Sinead Kinsella, Dr Saradha Srinivasan

Medlab Pathology, Unit 3, Sandyford Business Centre, Sandyford Business Park, Dublin 18

## 3. Measuring Glucose in Neonates

O'Kelly R, Stapleton M, O'Donnell A, O'Sullivan A, White M.

Coombe Women and Infants University Hospital, Dublin 8

## 4. A pilot study of serum biomarkers in Chronic Kidney Disease (CKD).

Griffin TP<sup>1,2\*</sup>, Islam MN<sup>1\*</sup>, Martin WP<sup>1,2</sup>, Cormican S<sup>3</sup>, Naicker SD<sup>1</sup>, Logue S<sup>1</sup>, O'Shea PM<sup>4</sup>, O'Brien T<sup>1,2</sup>, Griffin MD<sup>1,3</sup>.

<sup>1</sup>Regenerative Medicine Institute (REMEDI) at CÚRAM Centre for Research in Medical Devices, School of Medicine, College of Medicine, Nursing and Health Sciences, National University of Ireland, Galway.

<sup>2</sup>Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Saolta University Health Group, Galway.

<sup>3</sup>Nephrology Services, Galway University Hospitals, Saolta University Health Group, Galway.

<sup>4</sup>Department of Clinical Biochemistry, Galway University Hospitals, Saolta University Health Group, Galway.

\*Griffin TP and Islam MN contributed equally to this work.

## 5. Vitamin D Receptor TaqI Gene Variant in Exon 9 and Apal in Intron 8 in uncontrolled paediatric asthma in Ireland

Hutchinson K<sup>1,4</sup>, Kerley CP<sup>3</sup>, Cormican L<sup>2</sup>, Faul J<sup>2</sup>, Greally P<sup>3</sup>, Coghlan D<sup>3</sup>, Louw M<sup>1</sup>, Elnazir B<sup>3</sup>, Rochev Y<sup>4</sup>

<sup>1</sup>Biomnis Ireland, Sandyford, Dublin 18, Ireland.

<sup>2</sup>Asthma Research Centre, Connolly Hospital, Dublin 15, Ireland.

<sup>3</sup>Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland.

<sup>4</sup>School of Chemistry, National University of Ireland, Galway, Ireland.

## 6. Case Presentation - Can Amino Acid Analysis Contribute to Chemotherapy Management?

Deverell D<sup>1</sup>, Twomey A<sup>1</sup>, Fitzsimons P<sup>1</sup>, O'Shea, A<sup>1</sup>, McLoughlin, S<sup>2</sup>, McGovern, R<sup>2</sup>, Smith OP<sup>2</sup> and Mayne PD<sup>1</sup>

<sup>1</sup>Department of Paediatric Laboratory Medicine, Temple Street Children's University Hospital, Dublin. (TSCUH)

<sup>2</sup>Haematology Oncology Unit, Our Lady's Children's Hospital, Crumlin. (OLCHC)

## 7. Localisation of an Insulinoma; biochemistry superior to imaging

McDonnell TM<sup>1</sup>, O'Shea PM<sup>2</sup>, Bell M<sup>1</sup>

<sup>1</sup>Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway.

<sup>2</sup>Department of Clinical Biochemistry, Galway University Hospitals, Galway.

## 8. Evaluation of a Method for the Direct Measurement of Low-Density Lipoprotein Cholesterol in Serum

Walsh N, O'Shea P, Blake L, Kelly P, Griffin D

Department of Clinical Biochemistry, Galway University Hospitals, Saolta University Health Group, Galway

## 9. High prevalence of vitamin D deficiency observed in an Irish South Asian population

Laird E<sup>1</sup>, Carelton L<sup>2</sup>, Crowley VEF<sup>2</sup>, Healy M<sup>2</sup>

<sup>1</sup>School of Medicine, Trinity College Dublin

<sup>2</sup>Department of Biochemistry, Central Pathology, St. James's Hospital, Dublin

## 10. Severe Lactic Acidosis – an uncommon cause?

L. Kavanagh-Wright, B. Moran, B. Byrne, G. Reid, W. Tormey & G. Collier

Department of Chemical Pathology, Beaumont Hospital, Dublin 9

## 11. Pseudohyponatraemia: "We are not over the HIL"

Alice O'Brien<sup>1</sup>, Helen Kavanagh<sup>1</sup>, Maria Fitzgibbon<sup>1</sup>, Graham Lee<sup>1</sup>

<sup>1</sup>Clinical Biochemistry and Diagnostic Endocrinology, Mater Misericordiae Hospital, Dublin 7

## 12. An Unusual Diagnostic Outcome from a Pregnancy Test

Peadar McGing<sup>1</sup>, Eileen McMahon<sup>2</sup>, Emily Harrold<sup>2</sup>, Connor O'Keane<sup>3</sup>, Michaela Higgins<sup>2</sup>.

<sup>1</sup>Dept of Clinical Chemistry and Diagnostic Endocrinology,

<sup>2</sup>Dept of Medical Oncology,

<sup>3</sup>Dept of Pathology, Mater Misericordiae University Hospital, Dublin 7.

## 13. A Complex Case of Congenital Adrenal Hypoplasia

PE Fitzsimons<sup>1</sup>, E Lynch-Quinn<sup>1</sup>, E O'Ceallaigh<sup>2</sup>, N McGrath<sup>2</sup>, I Knerr<sup>3</sup>, D O'Rourke<sup>4</sup>, SA Lynch<sup>5,6</sup>, NP Murphy<sup>2,6</sup>, and PD Mayne<sup>1</sup>.

<sup>1</sup>Departments of Paediatric Laboratory Medicine,

<sup>2</sup>Paediatric Endocrinology,

<sup>3</sup>National Centre for Inherited Metabolic Disorders,

<sup>4</sup>Paediatric Neurology,

<sup>5</sup>Clinical Genetics, Children's University Hospital, Temple Street, Dublin 1,

<sup>6</sup>School of Medicine, University College Dublin, Dublin.

## 14. To D<sub>2</sub> or not to D<sub>2</sub>: medication mishap?

Murray H<sup>1</sup>, Griffin TP<sup>2</sup>, Blake L<sup>3</sup>, Bell M<sup>2</sup>, O'Shea PM<sup>3</sup>

<sup>1</sup>Department of Pharmacology & Therapeutics, National University of Ireland, Galway.

<sup>2</sup>Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway.

<sup>3</sup>Department of Clinical Biochemistry, Galway University Hospitals, Galway.

## 15. The Comparison of eGFR prediction Equations and mGFR using 51CrEDTA in Prospective Irish living Kidney Donors

E. Pentony, B. Byrne, M. Dooley, WP Tormey and G. Collier

Department of Chemical Pathology, Beaumont Hospital, Dublin

## 16. Retrospective Review of Pyrimidine Degradation Disorders in Ireland: Is it time for Guidelines on Screening for Fluoropyrimidine Toxicity?

PE Fitzsimons<sup>1</sup>, I Borovickova<sup>1</sup>, G Urbano<sup>1</sup>, AA Monavari<sup>2</sup>, PD Mayne<sup>1</sup>

<sup>1</sup>Department of Paediatric Laboratory Medicine, Temple Street, Children's University Hospital, Dublin 1, Ireland

<sup>2</sup>National Centre for Inherited Metabolic Disorders, Temple Street, Children's University Hospital, Dublin 1, Ireland

## 17. An Estimation of the Prevalence of Known Genetic Variants in the BCHE and UGT1A1 Genes in an Irish Population

Evan Keogh<sup>1</sup>, Sarah Savage<sup>1</sup>, J McPartlin<sup>2</sup>, Ronan Conroy<sup>3</sup> and Vivion E F Crowley<sup>1</sup>

<sup>1</sup>Biochemistry Department, St James's Hospital, Dublin 8

<sup>2</sup>IMM Biobank Trinity Centre, TCD School of Medicine, St James's Hospital, Dublin 8

<sup>3</sup>Division of Population Health Sciences, RCSI, Dublin



Bishop Lucey Park, Cork

## Poster 1

### *An unusual case of Pseudohyponatraemia*

**Maguire,OC<sup>1</sup>, Singh,K<sup>2</sup>, Barden,E<sup>3</sup> and McCormick,PA<sup>2</sup>**

<sup>1</sup>Department of Clinical Chemistry,

<sup>2</sup>Liver Unit, St Vincent's University Hospital, Dublin

<sup>3</sup>Department of Biochemistry, Mercy University Hospital, Cork

The most common causes of pseudohyponatraemia are severe hypertriglyceridaemia and hyperproteinaemia. Its association with isolated hypercholesterolaemia is less well known.

We report a case of a 66 year old women admitted with severe cholestatic hepatitis, believed to be due to sulfasalazine. LFTs on admission showed Total Bilirubin 742 umol/L (0-21), ALP 607 IU/L (30-130), GGT 1112 IU/L (6-40), ALT 242 IU/L (8-41). The sodium result of 119mmol/L ((133-146), Roche Cobas analyser) indicated hyponatraemia which did not fit with the clinical picture. Pseudohyponatraemia was confirmed by measurement of sodium by direct potentiometry (133mmol/L; Radiometer ABG analyser) and a normal serum osmolality (288 mmol/kg; 280-295) in the absence of other known osmotically active substances. Total protein was 57 g/L (60-80) and triglycerides were 4.0 mmol/L. Total cholesterol was significantly elevated at 38.9 mmol/L. The hypercholesterolaemia was due to the presence of Lipoprotein X (confirmed by Lipoprotein Electrophoresis) which is known to accumulate in the serum of patients with severe cholestatic liver disease.

The patient was treated with intravenous fluids, antibiotic(rifampicin),deflazacort and ursodeoxycholic acid. She improved clinically and bilirubin fell to 367 umol/L on discharge, 5 days later. Total cholesterol was 30.9mmol/L and pseudohyponatraemia was still evident (131 mmol/L, Roche Cobas v 140 mmol/L, ABG analyser). She was re-admitted two months later for management of severe pruritis. Total cholesterol had decreased to 20.5 mmol/L. Pseudohyponatraemia was not evident; however sodium was 5 mmol/L lower when measured on the Roche Cobas.

This case shows that the accumulation of Lipoprotein X particles in serum, as evidenced by extreme hypercholesterolaemia, can be a cause of pseudohyponatraemia. Inappropriate treatment of hyponatraemia with drugs such as vaptans may be hazardous. Serum sodium is one of the prognostic indices used to make decisions regarding liver transplantation. This case highlights the importance of being aware of uncommon causes of pseudohyponatraemia.

## Poster 2

### ***Title: An Analysis of Factors Influencing Sample Rejection Trends for Faecal Immunochemical Testing (FIT) in the Irish National Bowel Screening Programme***

**Halina Antonowicz, Ethna O'Shea, Sinead Kinsella, Dr Saradha Srinivasan.**

*Address: Medlab Pathology, Unit 3, Sandyford Business Centre, Sandyford Business Park, Dublin 18, Sandyford, Ireland*

#### **INTRODUCTION:**

Colorectal cancer represents a significant health problem. At present, Irish residents are offered a free Faecal Immunochemical Test (FIT) starting with men and women aged 60 to 69 in two yearly cycles under the National Bowel Screening Programme.

#### **AIM:**

The aim of this study was to examine the rejection rate and the reasons behind rejection of FIT samples.

#### **PATIENTS AND METHOD:**

126 068 samples were received over a 24 month period and were analysed on the OC-sensor Diana automated analyser. Data for all samples was collected, reviewed and analysed for the purpose of this study.

#### **RESULTS:**

Most samples received in the laboratory (123 950) were analysed and reported as negative or positive. 2118 samples (1.68 %) in total were reported as unsuitable for testing for different reasons. There are a numbers of reasons for why a sample would be deemed unsuitable. These reasons were categorised as being either pre-analytical or post-analytical. Most of the samples rejected (98%) were rejected due to pre-analytical reasons. Post-analytical reasons accounted for less than 2% of all rejected samples.

#### **CONCLUSIONS:**

Implementation of changes to the current working laboratory documents would be beneficial to re-evaluate rejection trends in the future i.e. formal categorization of reasons for rejection. Updated instructions with clearer picture diagrams may make it easier for the patient to follow instructions and could help in minimizing the number of misused samples being sent for testing. The findings from this project could be used as a guide in helping to minimize the rejection rate for the next round of screening in Ireland.

## Poster 3

### *Measuring Glucose in Neonates*

**O'Kelly R, Stapleton M, O'Donnell A, O'Sullivan A, White M.**

*Coombe Women and Infants University Hospital, Dublin 8.*

#### **OBJECTIVE:**

Neonates may be at risk of hypoglycaemia in the first few days after birth. In order to identify hypoglycaemia, blood glucose concentrations are measured - however to avoid unnecessary blood loss in this population and to provide a timely result, Point of Care (POC) devices are frequently used although discrepancies have been noted in the literature and may contribute to lack of confidence in the use of such devices. The aim of this study was to investigate whether glycolysis may contribute to these differences.

#### **STUDY DESIGN:**

Glucose measurement on 44 neonatal whole blood samples from 20 neonates using a glucose meter on the ward were compared with a central laboratory method using fluoride-heparinised plasma. In a second study, 30 fluoride-heparinised neonatal samples received in the laboratory within 20 minutes of phlebotomy were divided into two aliquots before centrifugation and analysis for plasma glucose – one analysed immediately and one left for one hour at room temperature before analysis.

#### **RESULTS:**

The mean ward meter result was 4.5 mmol/L while the mean laboratory result for the corresponding plasma glucose was 3.7 mmol/L.  $P < 0.0001$ . The mean glucose result for 30 neonatal fluoride-heparinised samples less than 20 minutes old was 4.1 mmol/L, while the mean glucose for aliquots of these samples left unseparated for one hour at room temperature was 3.7 mmol/L.  $P < 0.0001$ .

#### **CONCLUSION:**

Differences in glucose measurements in neonatal samples between ward glucose meters and the central laboratory may be partly due to glycolysis during transport in spite of the use of fluoride inhibition. Rapid separation, alternative glycolytic inhibitors or transport on ice should be considered for accurate laboratory glucose measurements.

## Poster 4

### *A pilot study of serum biomarkers in Chronic Kidney Disease (CKD).*

**Griffin TP<sup>1,2\*</sup>, Islam MN<sup>1\*</sup>, Martin WP<sup>1,2</sup>, Cormican S<sup>3</sup>, Naicker SD<sup>1</sup>, Logue S<sup>1</sup>, O'Shea PM<sup>4</sup>, O'Brien T<sup>1,2</sup>, Griffin MD<sup>1,3</sup>**

<sup>1</sup> Regenerative Medicine Institute (REMEDI) at CÚRAM Centre for Research in Medical Devices, School of Medicine, College of Medicine, Nursing and Health Sciences, National University of Ireland, Galway.

<sup>2</sup> Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Saolta University Health Group, Galway.

<sup>3</sup> Nephrology Services, Galway University Hospitals, Saolta University Health Group, Galway.

<sup>4</sup> Department of Clinical Biochemistry, Galway University Hospitals, Saolta University Health Group, Galway.

\* Griffin TP and Islam MN contributed equally to this work.

#### INTRODUCTION:

A significant unmet clinical need is the identification of biomarkers that serve as predictors or early indicators of both disease progression and favourable therapeutic response in Chronic Kidney Disease (CKD).<sup>1</sup>

#### AIM:

The aim of this study was to identify a panel of novel biomarkers which could be used to evaluate longitudinal trends in CKD.

#### METHODS:

Study subjects were identified from a prospectively maintained database/biobank. Subjects were divided into groups based on stage of CKD: stage 0/1 (eGFR  $\geq 90$  mL/min/1.73m<sup>2</sup>; n=19), stage 2 (eGFR 60-89 mL/min/1.73m<sup>2</sup>; n=17), stage 3 (eGFR 30-59 mL/min/1.73m<sup>2</sup>; n=40), stage 4 (eGFR 15-29 mL/min/1.73m<sup>2</sup>; n=37), stage 5 (eGFR  $< 15$  mL/min/1.73m<sup>2</sup>; n=7). Baseline demographics, metabolic and renal indices were recorded. The biomarkers selected for analyses were Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney Injury Molecule-1 (KIM-1), Adiponectin, Leptin, Fibroblast Growth Factor-21 (FGF-21), Plasminogen Activator Inhibitor (PAI-1), soluble Tumour Necrosis Factor-1 (sTNFR-1), soluble Tumour Necrosis Factor-2 (sTNFR-2), Interleukin-8 (IL-8) and Monocyte Chemoattractant Protein-1 (MCP-1). NGAL, KIM-1, Adiponectin, Leptin and FGF-21 were measured using respective Enzyme-linked Immunosorbent assay. Leptin:Adiponectin ratio (LAR) was calculated by dividing Leptin by Adiponectin. PAI-1, sTNFR-1, sTNFR-2, IL-8 and MCP-1 were measured by Bioplex-200 using Multiplex Immunoassay kits. Statistical analyses were performed using GraphPad Prism 6®.

#### RESULTS:

NGAL, Leptin, LAR, FGF-21, sTNFR-1, sTNFR-2, IL-8 and MCP-1 levels demonstrated an ability to distinguish subjects with different stages of CKD. KIM-1, Adiponectin and PAI-1 did not assist in identifying different stages of CKD. eGFR showed a significant correlation with NGAL ( $r = -0.453$ ,  $p < 0.001$ ), FGF-21 ( $r = -0.389$ ,  $p < 0.001$ ), s-TNFR-1 ( $r = -0.476$ ,  $p = 0.009$ ), s-TNFR-2 ( $r = -0.403$ ,  $p < 0.001$ ), IL-8 ( $r = -0.374$ ,  $p < 0.001$ ), Adiponectin ( $r = -0.212$ ,  $p = 0.026$ ), Leptin ( $r = -0.367$ ,  $p < 0.001$ ) and LAR ( $r = -0.247$ ,  $p = 0.010$ ). Its correlation with MCP-1 approaches significance ( $r = -0.201$ ,  $p = 0.077$ ) and with a larger sample size we feel this correlation would be significant.

#### CONCLUSION:

NGAL, Leptin, LAR, FGF-21, sTNFR-1, sTNFR-2, IL-8 and MCP-1 are potential novel biomarkers to track longitudinally in CKD.

## Poster 5

### ***Vitamin D Receptor TaqI Gene Variant in Exon 9 and Apal in Intron 8 in uncontrolled paediatric asthma in Ireland***

**Hutchinson K<sup>1,4</sup>, Kerley CP<sup>3</sup>, Cormican L<sup>2</sup>, Faul J<sup>2</sup>, Greally P<sup>3</sup>, Coghlan D<sup>3</sup>, Louw M<sup>1</sup>, Elnazir B<sup>3</sup>, Rochev Y<sup>4</sup>**

<sup>1</sup> Biomnis Ireland, Sandyford, Dublin 18, Ireland.

<sup>2</sup> Asthma Research Centre, Connolly Hospital, Dublin 15, Ireland.

<sup>3</sup> Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland.

<sup>4</sup> School of Chemistry, National University of Ireland, Galway, Ireland

#### **BACKGROUND:**

Asthma is a chronic heterogeneous respiratory disease and affects around one out of every five children in Ireland. Vitamin D receptor (VDR) polymorphisms have been associated with asthma risk. We aimed to investigate the impact of 2 VDR polymorphisms in asthma susceptibility in relation to vitamin D status and other biochemical and immunological indices in uncontrolled paediatric asthmatics.

#### **MATERIALS AND METHODS:**

45 uncontrolled asthmatic children and 57 healthy volunteers were studied. Outcome measured lung function, full blood count (FBC), biochemical and immunological parameters of allergy, immunity, airway and systemic inflammation. Serum 25-hydroxyvitamin D (25OHD), parathyroid hormone, albumin, total calcium, alkaline phosphatases, and phosphate, total IgE, IgA, and CRP were measured on the Abbott Architect ci8200. Eosinophil cationic protein was analysed on Phadia 250. Serum levels of Interleukin-10 (IL-10) and Cathelicidin antimicrobial peptide were determined by human ELISA. FBC was performed on the Sysmex XE-2100D. Genotypes of VDR TaqI and Apal were determined using TaqMan® assays on Applied Biosystems Real-Time PCR-7500. The software used for the statistical analysis was GraphPad Prism 5, Version 5.01.

#### **RESULTS:**

We found no association between genotypes and 25OHD levels, lung function and other biomarkers with the exception of IL-10 and White Blood Cells (WBC). IL-10 levels were significantly low in asthmatics with TC genotype for TaqI polymorphism and were significantly high in patients with TT genotype for Apal (p value < 0.005). WBC were significantly high in patients with TC and CC genotypes for TaqI and significantly low in TT genotype for Apal.

#### **CONCLUSION:**

Our report suggests that TaqI and Apal polymorphisms are associated with uncontrolled asthma in Irish children. Further studies are warranted to investigate the importance of decreased IL-10 levels in uncontrolled paediatric asthmatics with specific genotypes that could help us to understand the mechanism involved in the development of paediatric asthma.

## Poster 6

### **Case Presentation – Can Amino Acid Analysis Inform Chemotherapy Management?**

**Deverell D<sup>1</sup>, Twomey A<sup>1</sup>, Fitzsimons P<sup>1</sup>, O Shea, A<sup>1</sup>, McLoughlin, S<sup>2</sup>, McGovern, R<sup>2</sup>, Smith OP<sup>2</sup> and Mayne PD<sup>1</sup>**

<sup>1</sup> Department of Paediatric Laboratory Medicine, Temple Street Children's University Hospital, Dublin (TSCUH).

<sup>2</sup> National Paediatric Haematology & Oncology Centre, Our Lady's Children's Hospital, Crumlin.(OLCHC)

#### **PRESENTING ILLNESS:**

A 3y old girl with acute lymphoblastic leukaemia (ALL) was undergoing active treatment at OLCHC. Following an episode of hypoglycaemia, (glucose 2.5mmol/L), and an elevated ammonia (370µmol/L, Ref. <65), samples for a metabolic workup were referred to TSCUH

#### **LABORATORY FINDINGS**

Amino acid analysis revealed undetectable Asparagine (Asn) and Glutamine (Gln) levels. Acylcarnitine profiling showed a ketotic pattern consistent with lipolysis and markers of liver dysfunction. Urinary organic acid analysis supported these finding and no underlying inherited metabolic cause for the hypoglycaemia was evident.

#### **MEDICATION**

This child was receiving PEG-Asparaginase (PEG-Asp), the most efficacious Asparaginase formulation used in the treatment of paediatric ALL. Asparaginase degrades Asn, and to a variable extent Gln, consequently reducing their availability in tumour cells, which are highly dependent on these amino acids for proliferation. Prolonged use of this enzyme has been shown to be a risk for developing hyperammonaemia and associated morbidities.

#### **MODE OF ACTION**

Asn acts as an amino acid exchange and allows intracellular influx for the synthesis of nucleotides and proteins essential for cell division. Gln is necessary for anaplerosis of the TCA cycle in mitochondria and the high dependency of tumour cells on this amino acid is sometimes referred to as 'glutamine addiction'.

#### **INTERVENTION**

The use of PEG-Asp is the preferred asparaginase formulation in the treatment of paediatric ALL, however, it is not often that the amino acids are quantified. In our experience in one other patient with ALL, Asn was undetectable, but no concomitant reduction in Gln. These findings pose the question whether Gln levels could be a surrogate of efficacy of PEG-Asp therapy, and consequently a predictor of outcome.

#### **OUTCOME**

As the patient was not tolerating PEG-Asp well, she was switched to a different formulation of the enzyme, namely, Erwinase. This case prompts consideration for the monitoring of both ammonia and amino acids for evaluation of therapy.

## Poster 7

### *Localisation of an Insulinoma; biochemistry superior to imaging*

**McDonnell TM<sup>1</sup>, O'Shea PM<sup>2</sup>, Bell M<sup>1</sup>**

<sup>1</sup> Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway.

<sup>2</sup> Department of Clinical Biochemistry, Galway University Hospitals, Galway.

A 61 year old female presented to the emergency department (ED) with an episode of disorientation, confusion and slurred speech. On arrival to ED her blood glucose was 3.1 mmol/L (RI (Random): 3.9-7.8). Following an infusion of 20% dextrose her symptoms resolved. The patient described previous episodes of disorientation which had improved on eating. She also admitted to recent polyphagia and weight gain. Her background was significant for transient ischaemic attack (TIA), a prior hemi-thyroidectomy and an acoustic neuroma. Hyperinsulinaemia was confirmed 18 hours into a 72h fast. A plasma glucose of 2.2 mmol/L (RI (Fasting): 4.4-5.5) was concomitant with an inappropriately elevated serum insulin, 45.6 pmol/L (RI (Fasting): 17.8-173), C-Peptide, 569 pmol/L (RI (Fasting): 370-1470) and blood ketone ( $\beta$ -hydroxybutyrate) of 340  $\mu$ mol/L (Non ketotic: <600). A sulfonylurea screen was negative for the following drugs Chlorpropamide, Glibenclamide, Gliclazide, Glimepiride, Glipizide, Tolazamide and Tolbutamide. Following clinical and biochemical confirmation of hyperinsulinaemia, imaging was undertaken. Both computed tomography (CT) and magnetic resonance imaging (MRI) abdomen were inconclusive. An endoscopic ultrasound (EUS) identified a possible 0.8mm lesion at the head of the pancreas with a certitude of <80%. Diazoxide and later octreotide therapy was trialled but the patient continued to experience symptomatic hypoglycaemia. In order to further clarify the location of the insulinoma the patient was referred to St. Bartholomew's Hospital, London for a calcium simulation test. The rise in insulin levels in the superior mesenteric artery (SMA) and the gastroduodenal artery (GDA) following calcium injection, supported the endoscopy findings that the insulinoma was likely located at the head of pancreas. The patient subsequently went on to have a Whipple's resection with removal of the head of pancreas. Following surgery the patient had resolution of her symptoms. The case highlights the importance of biochemistry in the identification and localisation of an insulinoma.

## At The Frontier Of Medical Pathology

### Testing For Over 100 Years

Now, as part of the Eurofins Scientific global network of over 225 laboratories, Biomnis is proud to provide our clients with unrivalled access to an ever expanding portfolio of routine and esoteric tests. Our mission is to shape the future of medical pathology by providing all patients with the most specialised and innovative screening, diagnosis, monitoring and therapeutic adjustment techniques available throughout the globe. In partnership with you, we will help provide patient care that is among the best in the world.



Menu of Over 2,500 Routine & Esoteric Medical Laboratory Tests



Rapid Result Turnaround Times As We Manage the Entire Sample Collection, Testing and Reporting Pathway



Industry Leading IT Connectivity Solutions



Ireland's Largest Fleet of Specimen Transport Vehicles

## Poster 8

### ***Evaluation of a Method for the Direct Measurement of Low-Density Lipoprotein Cholesterol in Serum***

**Walsh N, O'Shea P, Blake L, Kelly P, Griffin D**

*Department of Clinical Biochemistry, Galway University Hospitals, Saolta University Health Group, Galway.*

#### **INTRODUCTION:**

Low-density lipoproteins are a heterogeneous population of particles that transport cholesterol to cells throughout the body. Elevated levels of low-density lipoprotein cholesterol (LDL-C) are associated with an increased risk of cardiovascular disease. LDL-C concentrations are therefore useful in estimating an individual's risk and in monitoring patients on lipid-lowering therapies. Rather than measuring LDL-C directly, most biochemistry laboratories use the Friedewald calculation to estimate it. The aim of this study was to evaluate a direct method for LDL-C determination.

#### **METHODS:**

The analytical performance specifications of the Roche LDL-C assay were assessed. A method comparison study between the Roche assay, the Friedewald equation and an Abbott direct LDL-C assay was performed on 60 patient samples. To assess its accuracy, we compared Roche assay results with those of putative gold-standard results (i.e. international standard reference material and specimens analysed by a  $\beta$ -quantification reference procedure).

#### **RESULTS:**

Precision at LDL-C concentrations of 1.72, 2.37 and 4.28 mmol/L was <2%. The method was linear to a concentration of 8.33 mmol/L. Using a higher order reference material, the inaccuracy of the method was 7.4% and 12.1% concentrations of 2.24 and 3.72 mmol/L, respectively. Comparison to  $\beta$ -quantification demonstrated inaccuracies of 5.42%, 18.92% and 0.27% at LDL-C concentrations of 1.66, 2.11 and 3.64 mmol/L.

#### **CONCLUSION:**

The Roche direct LDL-C method has satisfactory imprecision. However, the results did not accurately reflect those expected on analysis of gold standard materials, which suggests the method may benefit from re-calibration. The Abbott method showed the highest level of inaccuracy with the Friedewald equation proving the most accurate. While the study did not highlight any significant benefits over those achieved by the Friedewald equation, a follow-up study may be warranted to investigate whether the direct LDL-C method could provide added value in patients with hypertriglyceridaemia.

## Poster 9

### ***High prevalence of vitamin D deficiency observed in an Irish South Asian population***

**Laird E<sup>1</sup>, Carelton L<sup>2</sup>, Crowley VEF<sup>2</sup>, Healy M<sup>2</sup>**

<sup>1</sup>*School of Medicine, Trinity College Dublin*

<sup>2</sup>*Department of Biochemistry, Central Pathology, St. James's Hospital, Dublin*

#### **INTRODUCTION:**

Vitamin D deficiency (25(OH) D  $\leq$ 30 nmol/L) is a significant global health concern. At far latitudes, non-ethnic population groups from lower latitudes can be at a significantly increased risk of deficiency. The vitamin D status of ethnic minority groups has been examined extensively both in UK and European populations, but to-date, has not been investigated in the Irish context.

#### **METHODS:**

A search was conducted using the St James's Hospital Dublin Biochemistry Department LIS for vitamin D requests by GPs for individuals of Asian descent. Samples requested for the year 2011-2012 were selected (n=115). 25(OH)D concentrations were quantified using LC-MS/MS. Results were tabulated according to geometric mean values for vitamin D and by the percentage of samples deficient, insufficient (30-50 nmol/L) or normal ( $>$ 50 nmol/L).

#### **RESULTS:**

The median age was 31 years (age range: 2 -64 years) with 59.1% of the sample male. Overall, 79.1% of the total sample were vitamin D deficient, with 8.7% sufficient. Females had a significantly higher geometric 25(OH)D concentration than males (22.3 vs 16.3 nmol/L;  $P=0.005$ ) but both groups had a significant proportion with deficient status (88.2% & 66.0% respectively). In males only, no participant attained vitamin D sufficiency. A similar cohort sampled in 2015 showed continued severe vitamin D deficiency states in this population group.

#### **CONCLUSION:**

In this sample of Irish adults and children of South Asian descent, alarmingly, over 79% were vitamin D deficient, which is over 6 times the current deficiency rate for Caucasian Irish adults. Given the importance of vitamin D for bone health, this sub-population could be at a significantly increased risk of rickets, impaired bone metabolism and osteoporosis. In addition it has been suggested that vitamin D deficiency is implicated in a range of other adverse health outcomes including cardiovascular disease and cancer.

## Poster 10

### *Severe Lactic Acidosis – an uncommon cause?*

**L. Kavanagh-Wright, B. Moran, B. Byrne, G. Reid, W. Tormey & G. Collier**

*Department of Chemical Pathology, Beaumont Hospital, Dublin 9*

A 76 year old man presented to ED with vomiting, confusion/agitation and slurred speech and a GCS 14/15. He was hypothermic & hypotensive. His whole blood glucose was 4.4mmol/L. He was a Type 2 diabetic and co-morbidities included benign prostatic hyperplasia, asthma and hypertension. Arterial blood gas analysis identified a severe lactic acidosis pH 6.7; pCO<sub>2</sub> 6.76 kPa; HCO<sub>3</sub> 6.6 mmol/L; Lactate 25 mmol/L. Plasma osmolality was 346 mmol/L with osmolar gap 34 and anion gap 43. Toxicology screen was negative. Creatinine 356 µmol/L and urea 14.1 mmol/L and was assessed as AKIN 3. He continued to deteriorate and within hours his GCS had fallen to 3/15 and he was admitted to ICU.

Due to the strong clinical suspicion of ethylene glycol poisoning, a serum sample was sent for analysis by GC-MS and fomepizole therapy was commenced. He was placed on intravenous bicarbonate and haemodialysis.

Ethylene glycol and glycolic acid were undetectable in the serum. Blood sample was sent for metformin analysis. The serum concentration was 59.2mg/L (RR 0.1-4.0mg/L). The final diagnosis was severe lactic acidosis secondary to metformin overdose.

Lactic acidosis is a rare complication of metformin therapy, <0.06 events per 1,000 patient-years. Metformin is eliminated by the kidney, and impaired kidney function can cause raised plasma concentration of the drug. According to NICE guidelines (Type 2 diabetes in adults (2015)), serum creatinine >150µmol/L or eGFR <30ml/min/1.7m<sup>2</sup> are contraindications for its use.

It has been suggested that metformin associated lactic acidosis occurs when the triumvirate of 1) plasma accumulation of metformin due to renal impairment, 2) impaired hepatic lactate removal and 3) increased production/accumulation of lactate (e.g. sepsis, hypo-perfusion, circulatory dysfunction) coalesce. Published case studies and this case show metformin overdose, without liver failure can occur and may be a more common cause of lactic acidosis than previously regarded.

## Poster 11

### ***Pseudohyponatraemia: “We are not over the HIL”!***

**Alice O’Brien<sup>1</sup>, Helen Kavanagh<sup>1</sup>, Maria Fitzgibbon<sup>1</sup>, Graham Lee<sup>1</sup>**

<sup>1</sup>*Clinical Biochemistry and Diagnostic Endocrinology, Mater Misericordiae Hospital, Dublin 7*

#### **INTRODUCTION:**

Pseudohyponatraemia (PHNa) may be suspected for samples with visual turbidity and normal serum osmolality. Measurement of Haemolysis, Icterus and Turbidity (HIL) is however more accurate and used increasingly more than visual inspection. Correlations of Lipaemic Index (LI), an index of turbidity, and triglyceride concentration are reportedly poor but variable. It is also poorly characterised how varying lipid concentrations contribute to differences in sodium concentration measured by indirect and direct ISE ( $\Delta$ Na). Full assessment of the well-known volume displacement effect is likely precluded by lipoprotein size heterogeneity. Despite this limitation, we aimed to investigate the relationship of varying lipid, protein and LI and  $\Delta$ Na, to define thresholds for investigating pseudohypo (or normo)natraemia.

#### **METHODS:**

We combined prospective and retrospective data from concurrent results of plasma sodium (ISE: Indirect + Direct: [n=150], triglyceride [Tg: <1 to 36 mmol/L], cholesterol [Chol], total protein [TP] and HILs, following analysis on an Abbott Architect c16000. Results were also obtained from a one month analysis period (n=21569). Replicate analysis of plasma samples (normal Tg, C and TP) at 3 sodium concentrations (118, 142 and 155 mmol/L) showed  $\Delta$ Na of 0, 4 and 5 mmol/L.

#### **RESULTS:**

Overall, [Tg] and LI were poorly correlated ( $\rho = 0.45$ [95% CI: 0.42-0.47]. The mode  $\Delta$ Na was 3 (median = 4) mmol/L. For increasing  $\Delta$ Na, the average LI and Triglyceride increased however each parameter was poorly correlated with  $\Delta$ Na ( $\rho = 0.25$ ). For a  $\Delta$ Na of 7 mmol/L, the lowest LI was 1.08 but less than 0.1 for  $\Delta$ Na <6 mmol/L. Implementing such LI thresholds for investigation of pseudohyponatraemia, involving visual inspection and direct ISE measurements, would involve 2 and 164 samples/day for LI >1.01 or >0.1 respectively.

#### **CONCLUSION**

LI cannot be used alone for assessing possible pseudohypo/normo natraemia. A pragmatic algorithm comprising multi-parameter thresholds and visual assessment is essential.

## Poster 12

### *An Unusual Diagnostic Outcome from a Pregnancy Test*

**Peadar McGing<sup>1</sup>, Eileen McMahon<sup>2</sup>, Emily Harrold<sup>2</sup>, Connor O'Keane<sup>3</sup>, Michaela Higgins<sup>2</sup>.**

<sup>1</sup> Dept of Clinical Chemistry and Diagnostic Endocrinology,

<sup>2</sup> Dept of Medical Oncology,

<sup>3</sup> Dept of Pathology, Mater Misericordiae University Hospital, Dublin 7.

#### **INTRODUCTION:**

Beta-hCG (Human chorionic gonadotrophin) is a glycoprotein secreted by the syncytiotrophoblast cells of the placenta. Paraneoplastic ectopic secretion has been well described and  $\beta$ -hCG measurement is central to diagnosis and monitoring of gestational trophoblastic tumours and gonadal tumours. We describe a case where  $\beta$ -hCG pregnancy testing led to an unusual diagnosis.

#### **CASE HISTORY:**

A previously healthy 35-year-old female presented to our institution with right knee pain of 3 weeks duration.

Investigations revealed a high grade osteogenic sarcoma with infiltration of skeletal muscle. Chemotherapy with alternating cycles of high dose methotrexate and doxorubicin/cisplatin was planned. A pre-chemotherapy urinary pregnancy test was positive and a confirmatory plasma  $\beta$ hCG level was elevated at 1080 IU/L (day3). There was clinical concern that the patient was pregnant. History plus ultrasound ruled against pregnancy. Neither were subsequent plasma  $\beta$ -hCG levels consistent with pregnancy: day5=1271, day6=1034, day8=1025.

Literature review showed that ectopic hCG production by osteosarcoma was very rare but some cases have been reported. The patient's tumour biopsy was re-tested: immunohistochemistry for  $\beta$ hCG was negative, as were immunostains for HPL and PLAP.

HCG levels fell in response to chemotherapy and had normalised by the start of cycle 3. Levels remained low (<1.2 IU/L) for the remaining four cycles.

#### **DISCUSSION:**

Although the primary tumour was negative for hCG it is very likely the elevated plasma  $\beta$ -hCG level was due to metastatic tumour. HCG monitoring and half-life measurement supported chemotherapy-induced cell kill. Knowing this patient had  $\beta$ hCG-producing metastases, different from the primary, helped patient treatment.

The rarity of  $\beta$ hCG-producing osteosarcoma contributed to confusion about this woman's initial 'positive' pregnancy test. Clinical laboratory scientists and clinicians should be aware that  $\beta$ hCG ectopic production can be associated with any cancer and that where positive pregnancy tests do not match clinical findings ectopic  $\beta$ hCG production should be considered.

## Poster 13

### *A Complex Case of Congenital Adrenal Hypoplasia*

**PE Fitzsimons<sup>1</sup>, E Lynch-Quinn<sup>1</sup>, E O’Ceallaigh<sup>2</sup>, N McGrath<sup>2</sup>, I Knerr<sup>3</sup>, D O’Rourke<sup>4</sup>, SA Lynch<sup>5,6</sup>, NP Murphy<sup>2,6</sup>, and PD Mayne<sup>1</sup>.**

<sup>1</sup> Departments of Paediatric Laboratory Medicine,

<sup>2</sup> Paediatric Endocrinology,

<sup>3</sup> National Centre for Inherited Metabolic Disorders,

<sup>4</sup> Paediatric Neurology,

<sup>5</sup> Clinical Genetics, Children’s University Hospital, Temple Street, Dublin 1,

<sup>6</sup> School of Medicine, University College Dublin, Dublin.

#### **CASE-REPORT:**

A 13 day, non dysmorphic male infant presented with poor feeding and significant weight loss. He was born at term after an uneventful pregnancy, birth weight was 3.75 kg and discharged on day 2. Examination revealed a dehydrated infant with mildly hyperpigmented genitalia. He was hyponatraemic and hyperkalemic, suggestive of congenital adrenal hyperplasia (CAH). Electrolytes normalised on treatment with IV hydrocortisone and 0.9% saline; however, 17- $\alpha$ -hydroxyprogesterone level was normal (7 nmol/L, ref stressed infants: <40) and random cortisol was 106 nmol/L, making salt wasting CAH unlikely. Elevated ACTH (362 ng/L, ref 7-63) and plasma renin (>25 ng/ml/Hr, ref 6-8) levels confirmed primary adrenal failure. Urine steroid profile was consistent with congenital adrenal hypoplasia (AHC). He had transaminitis with pseudohypertriglyceridaemia (9.32 mmol/L, ref 0-0.85). A metabolic work-up showed elevated CK (5373 U/L, ref 20-155) and markedly elevated glycerol on urine organic acid analysis suggesting complex glycerol kinase deficiency (GKD) due to Xp21 contiguous gene deletion syndrome. A deletion in the 3p21.1 region of Xp21 was confirmed. His mother had a normal array confirming de novo occurrence. He was discharged on hydrocortisone, fludrocortisone and salt supplementation. On follow-up at 11 weeks, he had appropriate weight gain, normal electrolytes and has a regimen during intercurrent illness.

#### **DIAGNOSIS:**

Xp21 contiguous gene deletion syndrome is a rare condition comprising deletions in adjacent genes on chromosome Xp21 resulting in AHC, Duchenne muscular dystrophy (DMD) and GKD. Diagnosis is based on clinical and laboratory findings. Symptoms depend on deletion size and appear almost exclusively in males due to X-linked inheritance. Usually the first and most severe signs are of adrenal insufficiency.

#### **CONCLUSION:**

We present the first Irish reported case of Xp21 contiguous gene deletion syndrome. The disorder is rare; however, measurement of CK, triglycerides and urine organic acid analysis should be considered in a male infant presenting with adrenal insufficiency where CAH has been excluded.

## Poster 14

### *To D<sub>2</sub> or not to D<sub>2</sub>: medication mishap?*

**Murray H<sup>1</sup>, Griffin TP<sup>2</sup>, Blake L<sup>3</sup>, Bell M<sup>2</sup>, O'Shea PM<sup>3</sup>**

<sup>1</sup> Department of Pharmacology & Therapeutics, National University of Ireland, Galway.

<sup>2</sup> Centre for Endocrinology, Diabetes and Metabolism, Galway University Hospitals, Galway.

<sup>3</sup> Department of Clinical Biochemistry, Galway University Hospitals, Galway.

#### **CASE PRESENTATION:**

An 89-year old woman and nursing home resident presented to the Endocrinology Outpatient Department. She had been diagnosed with primary hyperparathyroidism in 2007 that was deemed unsuitable for surgery. This was medically managed on Mimpara (Cinacalcet) 60mg/day and vitamin D supplementation. On examination she was clinically stable, her BP was 135/90, haemoglobin 8.9 g/dL, eGFR 32 mL/min/1.73m<sup>2</sup> with absence of proteinuria and haematuria on urinalysis (stage 3B renal impairment). Her adjusted Calcium; 2.33 mmol/L (RI: 2.20-2.55), PTH; 213 ng/L (RI: 15-65), 25-OH Vitamin D; 635 nmol/L (Optimal: 75-125nmol/L) and 1.25 dihydroxy Vitamin D; 125 pmol/L (RI: 40-120). Vitamin 25-OH D was measured using liquid chromatography-tandem mass spectrometry. It is reported as total vitamin 25-OH D, the composite of the measured 25-(OH)D<sub>2</sub> and 25-(OH)D<sub>3</sub> values, in this case 588 nmol/L and 47 nmol/L respectively. Of note the lady was very animated over the cost of her Vitamin D supplementation (€240 per month) as she had just been told that she was no longer eligible for the medical card. This together with her markedly elevated 25-OH D result prompted a review of her medications. It was determined that two months prior to this clinic visit she had been prescribed Ergocalciferol (Vitamin D<sub>2</sub>) 1.25 mg or 50,000 units/day) in addition to Desunin (Cholecalciferol (Vitamin D<sub>3</sub>) 20 µg or 800 units/day). The Ergocalciferol and Desunin were immediately discontinued and care taken to ensure that all her medications came under the Drugs Payment Scheme. She is being followed-up monthly with bloods for calcium and PTH. In general, in elderly patients drug dose selection should be cautious reflecting the greater frequency of polypharmacy and decreased hepatic, renal, and cardiac function. It is likely that Cinacalcet together with the degree of renal impairment were protective of the potential toxic effects of this lady's overzealous vitamin D supplementation.

## Poster 15

### ***The Comparison of eGFR prediction Equations and mGFR using <sup>51</sup>CrEDTA in Prospective Irish living Kidney Donors***

**E. Pentony, B. Byrne, M. Dooley, WP Tormey and G. Collier**

*Department of Chemical Pathology, Beaumont Hospital, Dublin*

Living kidney donation has become part of the transplantation programme in Beaumont Hospital. Accurate measurement of GFR is critical in the selection of kidney donors and recommendations suggest GFR of 80mL/min/1.73m<sup>2</sup> is considered suitable for kidney donation<sup>1</sup>. The aim of the study was to compare measured GFR (mGFR) to estimated GFR (eGFR) using the following prediction equations: MDRD, CKD-EPI, Cockcroft –Gault Equation, the Gentian Cystatin C and the new CKD-EPI-Creatinine Cystatin Equations in potential kidney donors. We also compared 24hr urine creatinine clearance (CrCL) to mGFR which was used to assess renal function prior to the introduction of <sup>51</sup>CrEDTA methodology.

Subjects were injected with <sup>51</sup>Cr EDTA and plasma samples were drawn at 120, 150, 180 and 240 minutes post injection. Plasma clearance was calculated using the Brøchner-Mortensen with modification of the disappearance curves<sup>2</sup>.

80 subjects were enrolled in the study. The median level of mGFR in this cohort was 94.5 mL/min/1.73m<sup>2</sup>. Results showed a positive bias between Cockcroft–Gault eGFR of +26.2%; CKD-EPI-Creatinine & Cystatin C eGFR of +17% and Gentian Cystatin C had a bias of + 52.2%. MDRD showed a negative bias of -2.7 %; the CKD –EPI had a positive bias of + 5.7%. CrCL had a median difference of +49.2 mL/min to mGFR.

The median GFR in our cohort was 94.5mL/min/1.73m<sup>2</sup>. This value is lower than that obtained in studies using inulin clearance but concurs with studies suggesting that <sup>51</sup>CrEDTA underestimates GFR by approximately 15% compared to inulin in healthy individuals. The bias between eGFR and mGFR can result in discordancy at clinical decision levels of 80mL/min/1.73m<sup>2</sup>. From this study, the eGFR equations were deemed not acceptable to assess renal function in potential kidney donors. In addition, assessment of renal function by CrCL may result in overestimation of renal function compared to the gold standard method.

#### **REFERENCE:**

- (1) Andrew PA et al : Guidelines for living donor kidney transplantation . Transplantation 2012; 93(7) 666-673
- (2) Brøchner-Mortensen. Routine methods and their reliability for assessment of GFR in adults with special reference to <sup>51</sup>CrEDTA clearance. Dan Med Bull 1978; 25:181-202.

## Poster 16

### ***Retrospective Review of Pyrimidine Degradation Disorders in Ireland: Is it time for Guidelines on Screening for Fluoropyrimidine Toxicity?***

**PE Fitzsimons<sup>1</sup>, I Borovickova<sup>1</sup>, G Urbano<sup>1</sup>, AA Monavari<sup>2</sup>, PD Mayne<sup>1</sup>**

<sup>1</sup> Department of Paediatric Laboratory Medicine, Temple Street, Children's University Hospital, Dublin 1, Ireland

<sup>2</sup> National Centre for Inherited Metabolic Disorders, Temple Street, Children's University Hospital, Dublin 1, Ireland

#### **AIM:**

Fluoropyrimidines, such as 5-fluorouracil (5-FU), are commonly prescribed chemotherapeutic agents. Fluoropyrimidines, are metabolised by Dihydropyrimidine dehydrogenase (DPD), the first of three enzymes in the pyrimidine catabolic pathway; reduced or absent activity of this enzyme can result in severe symptoms such as myelosuppression, mucositis, neurotoxicity, diarrhoea and sometimes fatal toxicity. Patients with complete or partial Dihydropyrimidinase (DHP) or beta-Ureidopropionase ( $\beta$ -UP) deficiency are also at risk. We aim to determine the incidence and carrier frequency of this group of disorders in Ireland and whether screening prior to 5-FU treatment is warranted.

#### **METHODS:**

A 20 year retrospective review of patients diagnosed with pyrimidine catabolic defects initially by urinary organic acid analysis was performed.

#### **RESULTS:**

Six individuals from five families were diagnosed with DPD deficiency, one with DHP deficiency and four from two families with  $\beta$ -UP deficiency. Presentation shows phenotypic heterogeneity; two, possibly incidentally during hypoglycaemic work-ups, three during family screening and others during seizure, failure to thrive or autism work-ups.

Based on this review the incidence of pyrimidine degradation disorders in Ireland is 1:160,000 with a carrier frequency of 1:200.

#### **CONCLUSIONS:**

Pyrimidine degradation disorders are individually rare; 11 individuals from 8 families were identified with a deficiency in one of the three enzymes involved in pyrimidine catabolism over the 20 year period.

There is no consensus in Ireland or Europe on routine testing for a pyrimidine degradation disorder in patients prior to receiving fluoropyrimidines. DPD levels show high inter- and intra-individual variation; this variability is likely to influence response to 5-FU with respect to toxicity, resistance and efficacy. Identification of individuals with defects in pyrimidine catabolism could realize personalized medication in cancer chemotherapy with pyrimidine analogs; however, when there is conflicting genotype-phenotype relations should screening be genetic, biochemical or a combination approach?

## Poster 17

### ***An Estimation of the Prevalence of Known Genetic Variants in the BCHE and UGT1A1 Genes in an Irish Population***

**Evan Keogh<sup>1</sup>, Sarah Savage<sup>1</sup>, J McPartlin<sup>2</sup>, Ronan Conroy<sup>3</sup> and Vivion E F Crowley<sup>1</sup>**

<sup>1</sup> Biochemistry Department, St James's Hospital, Dublin 8

<sup>2</sup> IMM Biobank Trinity Centre, TCD School of Medicine, St James's Hospital, Dublin 8

<sup>3</sup> Division of Population Health Sciences, RCSI, Dublin

The A and K genetic variants in BCHE and the UGT1A1\*28 mutation in UGT1A1 are associated with the clinical conditions of succinylcholine-induced apnoea (suxamethonium sensitivity) and Gilbert's syndrome respectively. In addition, UGT1A1\*28 homozygosity has a reported association with severe toxicity to Irinotecan, an antineoplastic drug used in cancer chemotherapy. While both conditions are known to occur in the Irish population, to date no clear-cut prevalence data has been generated, and the current study sought to address this deficiency.

Allelic discrimination (AD) assays were successfully optimised using Applied Biosystems 7500 Fast Real-Time PCR platform for each of the three genetic variants. Percentage population prevalence was calculated including 95% binomial confidence intervals. DNA sample analysis was performed on a cohort of Irish blood donors (n=400) representing a total of 800 alleles examined.

Heterozygosity for BCHE A and K variants was identified in 3.25% and 33.8% of the study population respectively, while homozygous K genotype showed a prevalence of 5.5%. However, there were no homozygous A genotypes among the 400 study subjects. In relation to UGT1A1\*28, the population prevalence for heterozygous expression was 37.25%, while the homozygous genotype had a prevalence of 9.25%.

In conclusion, AD assays for the specific variants were successfully designed and optimised prior to analysis. The data generated in this study is consonant with previous reports in that the observed prevalence levels are comparable with those seen in other populations. Finally, to our knowledge this is the first report estimating prevalence of these variants in a specific Irish population.



**Personalized  
Solutions**

## **A HEALTHIER HOSPITAL BEGINS WITH A HEALTHIER LAB**



How can you help your healthcare system grow? Abbott is dedicated to partnering with you to elevate the health of your healthcare institution. With our personalized solutions consisting of resourceful advocates, harmonized systems, and intelligent insights, we are focused on helping you achieve measurably better healthcare performance.

**For more information, please visit [AbbottDiagnostics.com](https://www.AbbottDiagnostics.com), ask your local Abbott Ambassador, or send an email: [wired@abbott.com](mailto:wired@abbott.com)**

**CHOOSE TRANSFORMATION**

**Clinical Chemistry | Immunoassay | Hematology | Transfusion | Molecular | Point of Care | Professional Services**



**Association of Clinical Biochemists in Ireland**  
[www.acbi.ie](http://www.acbi.ie)