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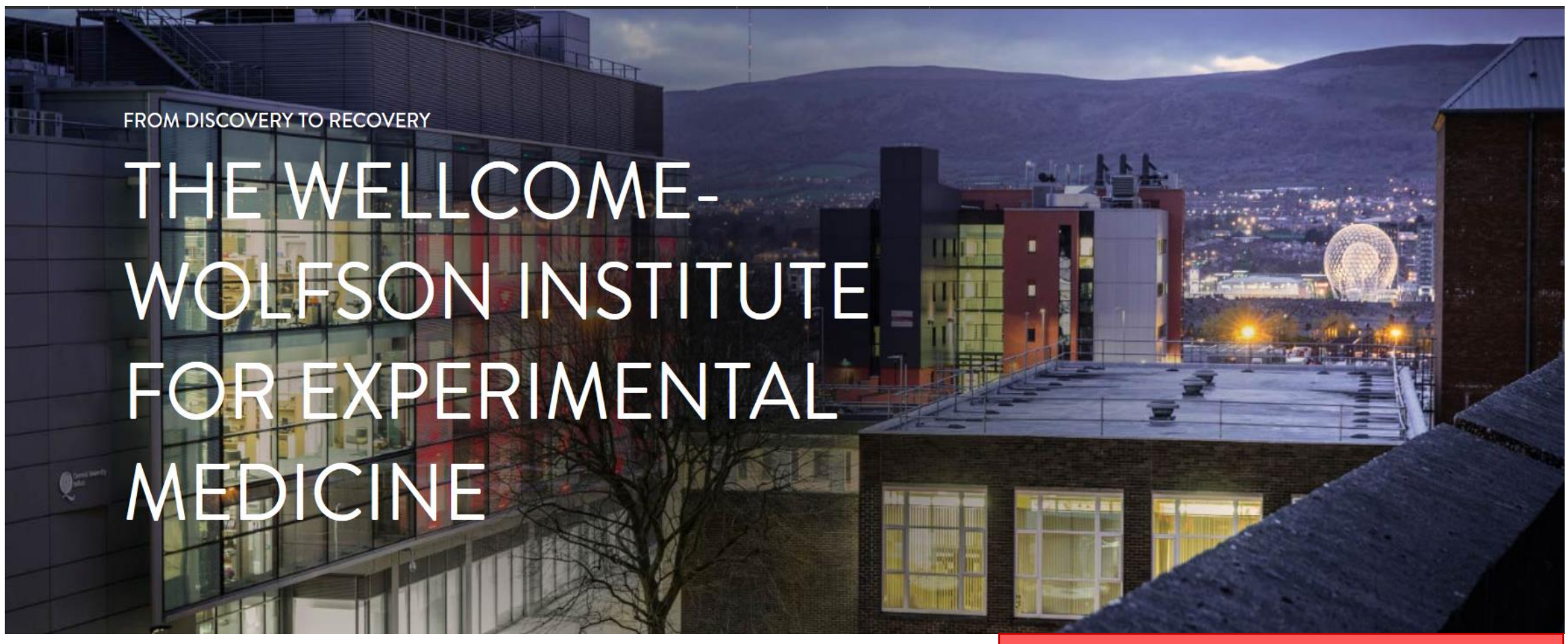
THE INVESTIGATOR



PROFESSOR JOSE A. BENGOECHEA

WWIEM DIRECTOR

Welcome to this new issue of the Investigator.

The first quarter of this academic year is ending, and we are delighted to have advanced in our priorities as a research institute: delivering high quality research in Experimental Medicine, but also to train the next generation of researchers and clinical academics.

We have welcomed to the labs research students both from our MSc Experimental Medicine, as well as from the MSc of Parasitology and Pathogen biology (School of Biological Sciences).

One of our priorities as a leading Experimental Medicine Research Institute is to consolidate the continuum from lab bench to patient's bed. Clinical academic appointments are central for us to succeed in this ambition. As part of this strategy, we are proud to have attracted three new clinical academics Professor Frank Casey, Dr Tom Waterfield, and Dr John Silversides. Our role in training future clinical academics is also part of our commitment, and it shows in the currently ongoing Academic Clinical Lecturers (ACLs) and Academic Clinical Fellows (ACFs) projects.

WWIEM has established collaborations with colleagues and institutions from the Republic of Ireland. Aligned with Strategy 2030, we focus on greater UK/Ireland research partnerships. Examples are our role in "Creating our future"; and how well positioned we were when the North South Research Programme was launched. It translated into 15 applications from the Institute, from all our research areas, under all the call Strands. Our ambition is to develop these collaborations to deliver impact and future economic growth.

IN THIS ISSUE

MEET OUR RESEARCHERS

Dr Anna Krasnodembskaya

Krasnodembskaya's research group works with Mesenchymal Stem Cells (MSC) with the particular focus on the MSC based cell therapy for Acute Respiratory Distress Syndrome (ARDS). ARDS constitutes a spectrum of severe acute respiratory failure and is leading cause of morbidity and mortality in critically ill. Our central goal is to understand how MSC work in the context of the injury microenvironment, how MSC modulate reparative capacities of the host cells and if we can enhance MSC therapeutic potential. We hope that this research will allow to develop better cell therapies as well as to identify new therapeutic targets for ARDS and sepsis. The current research projects are investigating effects of MSC on pulmonary macrophage polarisation, MSC modulation of distal lung endothelial and epithelial cell functions and more recently we became interested in therapeutic potential of MSC-derived extracellular vesicles as a potential cell-free therapy.

Dr Ikhlas el Karim

The goal of my research is to develop minimally invasive, biologically based therapies for inflammatory dental diseases. I have particular interest in investigating the link between pain, inflammation and regeneration as well as the implications of dental disease on general health. The current research programmes include:

1- Exploring potential strategies for optimal differentiation of dental pulp stem cells with particular focus on inflammation and its impact on regeneration

2- Developing in vitro and in vivo models to study neuronal signalling in inflammatory and neuropathic pain

3- Investigate potential links between dental infections, systemic inflammation and general heath.

Professor Ultan Power

Human respiratory syncytial virus (RSV) is the leading cause of bronchiolitis and pneumonia in infants worldwide and also causes considerable morbidity and mortality in the elderly and immunecompromised individuals. Re-infections are common throughout life. Despite more than 50 years of research there are no vaccines or specific therapeutics against RSV. Importantly, the mechanisms by which RSV causes disease in humans remain poorly understood.

The Power group has developed models of RSV infection based on well-differentiated primary paediatric airway epithelial cell cultures (WD-PAEC), the primary targets of RSV infection *in vivo*. These cultures are derived from both bronchial and nasal brushes of airway epithelium in ethically approved protocols. Our RSV/WD-PAEC model derived from bronchial epithelium demonstrated remarkable similarities to hallmarks of RSV infection in infant lungs, both at the cellular and molecular levels. This research indicated that our model provides an authentic surrogate for RSV infection of lower airway epithelium *in vivo*. Similarly, our RSV/WD-PAEC model derived from nasal epithelium provided the means to comprehensively study RSV infection in authentic paediatric upper respiratory tract epithelium tissue.

Dr Mei Chen

My research has been focused on the role of inflammation in the pathogenesis of retinal degenerative and angiogenic diseases, including age-related macular degeneration (AMD), diabetic retinopathy (DR) and Retinitis Pigmentosa (RP). Although AMD, DR and RP are not classical inflammatory diseases, inflammation is known to play an important role in the initiation and progression of the diseases. **Main research activities**

1) **Inflammation in DR:** We are interested in how diabetes affects immune cells and why the immune response to diabetes-mediated retinal injury becomes detrimental in DR. 2) **The role of Muller cell in retinal neurovascular unit:** The blood-retinal barrier (BRB) is essential for retinal immune privilege. The functional integrity of BRB is maintained by the retinal neurovascular unit. Muller cell, the principal glia spanning almost the entire retina, is an important component of the neurovascular unit. We aim to understand the regulatory role of Muller cells in the neurovascular unit and BRB, and how the regulation is altered in diseases such as DR and AMD. 3) **Topical drug delivery for the treatment of retinal diseases:** Due to the distinct anatomy of human eyes, it has been very difficult for topically applied drug to reach the posterior segment of the eyes.

NEW CLINICAL ACADEMICS APPOINTMENTS

Professor Frank Casey

On 1st September 2021, I took up the position of Clinical Professor of Paediatric Cardiology, a new joint appointment across Queen's University, Ulster University and Belfast Trust. This post was created by the All-Island Paediatric Cardiology Network and my task is to establish an Academic Department of Paediatric Cardiology and develop research in this field on an All-Island basis through collaborative projects.

I am a highly experienced Clinician, having worked in the Belfast Trust as a Consultant in Paediatric and Fetal Cardiology since 1996. My main areas of clinical expertise are in Fetal Cardiology and inherited cardiac conditions.

Since 2015 I have been the Northern Ireland Clinical Lead for the All-Island Paediatric Cardiology network and have been a key figure in its development and implementation. I am recognized internationally as a leader in research of Neurodevelopmental outcomes for children with congenital heart disease and also in the applications of E-Health and Telemedicine applications to the field of Paediatric Cardiology.

Internationally I am closely involved with the Association for European Paediatric Cardiology, and with the Cardiac Neurodevelopmental Outcomes Collaborative in the U.S.A. I am a member of the organizing committee of the World Congress of Paediatric Cardiology.

My research in Queen's will focus on further study of the neurodevelopmental outcomes for children post open heart surgery for congenital heart disease. In particular we will aim to develop interventions to optimise quality of life for this patient group. I will also have a focus on genomics in the Inherited cardiac conditions that are a cause of sudden cardiac death in young people.

Dr Tom Waterfield

I graduated from Oxford University Medical School in 2008 and subsequently completed my Paediatric Emergency Medicine (PEM) subspecialty training in Northern Ireland. I am a clinical academic with a Consultant contract at the Royal Belfast Hospital for Sick Children. I completed a PhD at Queen's University Belfast. My thesis focussed on the diagnosis of invasive Meningococcal Disease (MD) in children including the role of novel diagnostics including rapid molecular diagnostics. On completion of my PhD I subsequently worked as an Academic Clinical Lecturer at Queen's University Belfast before taking a Clinical Lecturer position at the WWIEM. My research interests are severe paediatric infections including Meningococcal Disease, Bacterial Sepsis and Covid-19. My research focus is on the early recognition and treatment of these infections including the development of novel diagnostics, mechanistic research and translation of this research including clinically meaningful outcomes for children. These outcomes include reducing treatment delays, minimising invasive procedures and good antimicrobial stewardship. I am an editor for Archives of Disease in Childhood and Vice-Chair of the Paediatric Emergency Research UK and Ireland network.

NEW CLINICAL ACADEMICS APPOINTMENTS

Dr Jonathan Silversides

I graduated in Medicine from Queen's University Belfast in 2002, having completed an intercalated degree in Medical Genetics. After some basic training in general medicine and emergency medicine, I specialised in anaesthesia and then Intensive (Critical) Care Medicine, completing my training in 2013. I spent time undertaking a fellowship in critical care medicine at the University of Toronto, where I developed an interest in clinical research. I have been working as a consultant in critical care and anaesthesia for the Belfast Trust since 2013, completing a part-time PhD with Danny McAuley and Bronagh Blackwood in WWIEM between 2015 and 2019. My research interests are based on clinical challenges that I encounter in my patients. One of these is the role of fluid therapy in sepsis and other critical illnesses: intravenous fluids are given to treat haemodynamic instability, but accumulation of fluid leads to tissues oedema and is associated with worse outcomes.

I completed a randomised feasibility trial of 'deresuscitation' – prevention and treatment of fluid overload to improve tissue oxygenation and patient outcomes as part of my PhD – this has led to a large NIHR-funded trial. I am now working on industry-supported studies to investigate ultrafiltration (mechanical fluid removal) in critically ill patients. In parallel to these clinical trials, I plan to use a human intravenous LPS model to investigate the mechanisms by which intravenous fluids and other therapeutic agents affect the microcirculation and systemic inflammatory response in sepsis. Another research theme is prevention of post-operative pulmonary complications, an area in which I have recently been awarded NIHR funding for a large randomised clinical trial.

Academic Clinical Fellows (ACF) and Academic Clinical Lecturers (ACL) at WWIEM

Clinical training offers a wide range of opportunities in programmes that have a strong track record in specialty training and academic activities.

Queen's University Belfast in partnership with the Northern Ireland Medical and Dental Training Agency and the Health and Social Care Trusts provide Clinical Academic Training opportunities in research and education. These posts offer candidates a comprehensive experience in clinical academic medicine alongside internationally recognised clinicians and researchers.

The ACL post is normally for 3 years. Those appointed at ACL level will be an existing Specialist Registrar who have completed a PhD or be within six months of submission at time of interview. They will finish their clinical training while continuing academic development at post-doctoral level with 50% research time at QUB. It is expected that trainees at this level will apply for an externally funded clinician scientist programme to extend their research to a consultant appointment.

The ACF post is normally for 2 years. During this period it is expected that the ACF will participate in clinical training with an integrated period of 25% of whole time equivalent academic research training in the specialty to which they are appointed. They will prepare an application for an externally funded clinical research training fellowship to undertake a PhD.

Trainees should review the Job Description for the specific criteria. Core clinical competencies will be gained as necessary through access to the essential elements of the training curriculum. Clinical training offers a wide range of opportunities in programmes that have a strong track record in specialty training and academic activities.

WWIEM hosts a number of ACL and ACF as part of our tradition to support the development of clinical academics.

Currently, WWIEM hosts the following ACLs and ACFs:

Trainee	Type of Post	Specialty	Centre	Academic Supervisor
McCarron, Eamonn	Academic Clinical Fellow	Chemical Pathology	WWIEM	Professor David Grieve & Dr C Watson
Linden, Dermott	Academic Clinical Lecturer	Respiratory	WWIEM	Professor Cliff Taggart
Groves, Helen Dr	Academic Clinical Lecturer	Paediatrics	WWIEM	Dr Damian Downey
Reddy, Kiran	Irish Clinical Academic Training	Anaesthesia/Intensive Care	WWIEM	Professor DF McAuley

Barcroft Lecture

The next 23 March 2022 Professor Pascale Cossart, Institut Pasteur, Paris will be presented the Barcroft Medal by the School of Medicine, Dentistry and Biomedical Sciences, in a lecture rescheduled due to the COVID 19 pandemic. (She was awarded the Barcroft Medal 2020).

Professor Cossart is a bacteriologist, foremost authority on *Listeria monocytogenes*. Prof Cossart pioneered a new research field, cellular microbiology, and her work has led to major landmark discoveries that have transformed our understanding on how pathogens manipulate our cells to survive.

Cossart earned a B.S. and M.S. from Lille University in 1968. She then earned an M.S. in chemistry from Georgetown University in 1971, and her Ph.D. in biochemistry at the Pasteur Institute and the University of Paris in 1977 (University Paris Diderot). She completed her postdoctoral fellowship at the Pasteur Institute. She is currently a Professor and Head of the Unité des Interactions Bactéries Cellules at the Pasteur Institute. In 1998, she received the Richard Lounsbery Prize and the L'Oreal-UNESCO Award for Women in Science. She was awarded the Balzan Prize for Infectious Diseases: Basic and Clinical Aspects in 2013.

Frederick W Price Memorial Lecture

November 8th, the last Frederick W Price Memorial Lecure. This lectureship was founded in 1944 by Dr Frederick W Price, London, to promote a closer association between the Faculty of Medicine at The Queen's University of Belfast and the medical profession in England, especially in London and is triennial.

This years recipient was Professor Edwin Chilvers *[BMedSci, BMBS, MRCP, PhD, FRCPE, FRCP, MA, FHEA, ScD, FMedSci]*

Professor of Medicine and Head of the National Heart and Lung Institute, Imperial College London. Edwin Chilvers is Professor of Medicine, and Head of the National Heart and Lung Institute (NHLI), at Imperial College London. His research interests are in inflammatory cell biology, in particular the intracellular signals that regulate the activation and survival of neutrophils and eosinophils.

This has translational relevance to a range of inflammatory lung diseases including chronic obstructive pulmonary disease (COPD), asthma and acute lung injury. He has a particular interest in the signalling mechanisms regulating NADPH oxidase function in neutrophils, and the control of neutrophil and eosinophil survival by hypoxia and inflammatory cytokines. His research has received continuous MRC and Wellcome Trust support for the past 25 years.

Professor Chilvers was Professor of Respiratory Medicine at Cambridge from 1998-2018 prior to taking up his current post, where he helped develop the academic Respiratory Medicine Division within the Department of Medicine and specialist clinical services at Addenbrooke's Hospital.

Barcroft lecture
23 March 2022
Professor Pascale Cossart

Prof Bengoechea, member of the Expert committee on #creating our future: a national conversation on research in Ireland

Creating Our Future is an initiative launched on 28 July 2021 by An Taoiseach Micheál Martin TD and Minister Simon Harris TD. This initiative seeks to initiate a national conversation about research in Ireland.

An Expert Committee has been established to lead the analysis and interpretation of ideas submitted by the public as part of the Creating Our Future campaign.

The newly established committee, composed of experts across a range of research disciplines, will lead the analysis and interpretation of submissions from the public dialogue. Under their leadership, five multidisciplinary Expert Working Groups will be established to support the analysis of the public's submissions.

Chaired by Professor Linda Hogan, Trinity College Dublin, the overarching purpose of the committee's analysis is to ensure that the findings reflect the public's voice and recommendations are developed to inspire research in Ireland.

Other members of the committee include Dr Niall Smith, Munster Technological University, Ms Lorna Ross, VHI Chief Innovation Officer, Dr Orla Flynn, Galway-Mayo Institute of Technology, Professor David Farrell, University College Dublin, Professor Brian Norton, the International Energy Research Centre, and Professor Anita Maguire, University College Cork.

All responses submitted to the portal will be collated and shared with independent experts, comprised of researchers from academia, the private sector, and civil society, who will distil the ideas into a report for Government to inspire future research in Ireland. Prof Bengoechea chairs the Expert Working Group focusing on Health and Wellbeing.

Professor Lois, appointed by NICE for the committee for the development of the Diabetic Retinopathy Guidelines

NICE selected Professor Lois me to support the works of the development of the NICE Diabetic Retinopathy Guidelines. These guidelines will determine how people with diabetes and diabetic retinopathy are looked after not only in the UK but across the world, as many countries look at the advice of NICE. They will be based on best available evidence.

Dr Rebeca Coll, receives Regeneron New Investigator Award for Excellence in Cytokine & Interferon Research

Dr Rebeca Coll was awarded the New Investigator Award for Excellence in Cytokine & Interferon Research by the International cytokines and Interferon Society. The award recognizes individuals who have made notable contributions to either basic or clinical research

North-South Research Programme

The Higher Education Authority (HEA) is delivering a special collaborative research funding programme, the North South Research Programme. As part of the Irish Government's Shared Ireland Initiative, €40 million of funding will be made available over 5 years to support research, innovation and development in North-South collaborative projects between individuals, research teams and institutions.

To accommodate different types of collaborations, the call was open for applications into one of three strands, with projects varying in size from up to €100,000 to €4,000,000.

Strand I: Bilateral researcher-researcher projects. This strand will support individual researchers with one based in a HEI in Northern Ireland and other in Ireland.

Strand II: Emerging hubs of excellence. This strand will support academic research teams to collaborate on an agreed work programme.

Strand III: Partnerships of scale. This strand will support institution to institution strategic research engagement.

The first call for this programme closed in November, and 15 North-South collaborative research projects were submitted from the Institute to this Programme.

4 applications for the Strand I include projects focusing on:

- Investigation of porcine reproductive and respiratory syndrome virus co-infection on hepatitis E virus infection of pigs
- Computations and biological investigation of mechanosensitivity in regulatory T cell development
- Understanding zinc biology in age-related macular degeneration (AMD) using nanotechnology-based local targeted
- SeeDeepER (Decoding Molecular circuitry underlying epilepsy)

9 applications for the Strand II include projects focusing on:

- All Island Pluripotent Stem Cell Platform for Development of Novel Therapies in Intractable Childhood-Onset Diseases
- Blocking bovine respiratory disease viruses using novel vaccine platforms - 'BRDBLOCK'
- Irish Green Labs
- Extracellular vesicle-based therapies for critical illness – developing an All-island advanced medicines accelerator
- Detection of Depth-Resolved Nanoscale Tissue Changes in the Retina and Choroid for RiskPrediction, Early Disease Diagnosis and Patient Stratification
- An All-Ireland approach to optimise digital healthcare management of long-term respiratory conditions
- All-Ireland Multiple Sclerosis Research Postdoctoral Academy
- Network of Excellence for Body-on-a-Chip Technology (NBCT)
- InterNeuro Ireland –Multidisciplinary Investigation of neurodevelopmental disorders-

2 applications for strand III include projects on:

- Healthtech Innovation Platform Ireland; Developing Products and People
- Irish Centre for training in Infectious Disease (ICID)

WWIEM Seminar series 2021

The Wellcome-Wolfson Institute for Experimental Medicine hosts research seminars from a range of renowned international experts. During lockdown they continued virtually. It was the best option to keep scientific discussions ongoing. Although the face to face interaction was missed, in it resulted in a great seminar season, as online sessions allowed us to bring in some of the best researchers in the world.
Our Seminars take place on Tuesdays at 1pm. They are open to all Queen's University Belfast staff and students and to members of the general public.

July

- Professor John Varga, Univiersity of Michigan, "Understanding the complex pathogenesis of systemic sclerosis“

September

- Dr Daniel Saban, Duke University School of Medicine, “Unraveling Niche-Specific Function of Microglia Using the Mouse Retina”
- Professor Andreas M Grabucker, University of Limerick, “Understanding abnormal Zinc signalling in Autism Spectrum Disorders and its potential as therapeutic target using Nanomedicines”
- Professor Bronagh Blackwood, WWIEM, "Design and evaluation of a change in clinical practice using a pragmatic trial design. The SANDWICH trial"

October

- Dr Salvador Macip, University of Leicester "Killing cells to live longer (and better) – The new revolution in anti-ageing research“
- Dr Felix Randow, MRC Laboratory of Molecular Biology
- Special Seminar: Dr Susana Salcedo, Université de Lyon, “Studying bacterial TIR effectors: from host immune evasion to bacterial warfare”
- Professor Ben tenOever, New York University, "A molecular basis for Long COVID"

November

- Dr Fiona Wilkinson, Manchester Metropolitan University "Endothelial microvesicles: pathogenic or passive players in vascular disease?”
- Professor Deborah Henderson, Newcastle University, “Novel genes, pathways and processes involved in arterial valve development in mouse and man”
- Neuroscience Day Keynote Speaker: Professor Beth Stevens, Boston Children's Hospital, Harvard Medical School, “(Re) Defining Microglia States, Function and Dysfunction in Disease”
- Dr Kate Fitzgerald, University of Massachusetts; 'Nucleic acid sensing pathways in infection and inflammatory disease'

December

- Professor Caroline Hill, The Francis Crick Institute; “The Ups and Downs of TGF-β Family Signalling” Microsoft Teams Meeting
- Dr Beckie Ingram, WWIEM, "Immunological memory of bacterial infections”

Post Doctoral Career Development Committee (PCDC)

For the second part of 2021, the PCDC has implemented the following initiatives:

Annual WWIEM Postdoctoral Research Symposium - This event is a celebration of WWIEM PDRAs and the excellent research they produce. The postdoc research symposium was held virtually this year, a first for the centre. The symposium took place over 2 half-days. The PCDC attracted high calibre external keynote speakers, Dr. Annie Curtis (RCSI), Dr. Luke Garret (University of Western Australia) and Prof Tony Wyss-Coray (Stanford University).

Career Insight Seminars - The Career Insight Seminars were piloted by the WWIEM PCDC in June 2020. Since then the PCDC have hosted 10 academic and non-academic speakers from careers ranging in project management, digital health, industry research and clinical trials management. Due to the success of the Career Insight Seminars, the PCDC have expanded Career Insight Seminars across all faculties, with different schools now hosting a seminar each month

Postdoc Coffee Mornings - Postdoc coffee mornings are held once a month via Teams. These meetings are now more structured, with different (non-work related) topics being discussed at each coffee morning.

Buddy Scheme - This scheme involves individually welcoming every new PDRAs within the centre. This postdoc run scheme offers an opportunity to orientate new PDRAs to the running of the centre and we provide a welcome pack with useful information including local amenities, accommodation and getting a bank account.

Given the recent global health emergency, this scheme has run virtually but will continue in person with social distancing.

Mental Health First Aid - As of 2019 the WWIEM PCDC in collaboration with faculty PDC, has provided volunteer PDRAs with Public Health Agency an accredited Mental Health First Aid (MHFA) qualification. Resulting in a set of trained PDRAs who have volunteered to be contacted by staff and students when required.

WWIEM Seminar Series - PDRA representatives are now a part of the WWIEM Seminar Series committee, as such we now have two dedicated PDRA-assigned seminar speaker slots. two dedicated PDRA-assigned seminar speaker slots.

Postdoc Career Away Day - This annual event, organised by the PCDC, is a fun PI-free day where we can check on PDRA wellbeing within the centre and offers an opportunity to network. During this event we provide a short training session requested by internal poll and hold a town hall session to flag any issues which need addressed in order to improve our the PDRA experience within WWIEM. 2021 away day was held over two consecutive mornings online.

PCDC Website
https://www.qub.ac.uk/research-centres/wwiem/EducationandTraining/PostdoctoralDevelopmentProgramme/

Amy Dumigan won an award for her oral presentation at 2021 Host-pathogen communications conference at the recent Ireland-Israel-Denmark meeting on Host-Pathogen Communication (https://www.weizmann.ac.il/conferences/HPC2021/)

PhD Students

In terms of academic developments, 1st Years did a great job at presenting their projects to the centre on Monday 22nd November.

The Postgrad Research Forum will be split over two days this year in Riddle Hall, with 3rd year student presentations 7th December and 2nd year student posters 8th December.

A pumpkin carving competition was initially set up for the PhD students throughout the centre but quickly developed to include everyone and was a successful event attended by many. Hershey's smores kits were given away as prizes: (1st Andriana Margariti group, 2nd Jose Bengoechea group, 3rd Chris Watson group)

•PhD & Postdoc reps have combined forces to introduce the 'WWIEM Wee Library' to promote well-being and sustainability within the centre. We ask that people donate a book when they take a book to keep everyone relaxed and well-read until more social activities can recommence.

•Coffee mornings for PhD students have now been moved to the basement seminar room and has encouraged more students to attend (we try to do this virtually alongside but the execution isn't too great on that side!).
There are other plans for social events in the future once/if the social restrictions ease, none the less, there are plans for movie nights and more outdoors events planned. Unfortunately, due to COVID restrictions traditional WWIEM Christmas activities, such as the famous 'Egg Drop', won't be going ahead this year.

Chloe McKee (3rd year PhD student) won a prize for best poster at the recent Ireland-Israel-Denmark meeting on Host-Pathogen Communicationn TCD (https://www.weizmann.ac.il/conferences/HPC2021/)

Grants and awards

MRC
Investigating the role of perivascular mesenchymal stem cells in retinal fibrosis secondary to neovascular age-related macular degeneration (nAMD)
PI: **Heping Xu**
Co-I: Mei Chen; Anna Krasnodembskaya
Funded value: £747,840

Age-related macular degeneration (AMD) is a disease that affects the central part of the back of the eye, the macula, causing progressive loss of central vision in the elderly. There are two advanced forms, wet and dry. Wet AMD is due to the growth of diseased blood vessels into the macula causing leakage and bleeding that damage vision. Approximately 200 million people are affected by AMD globally and this number is expected to increase to 300 million by 2040. AMD is the most common cause of blindness in the elderly of developed countries and wet AMD accounts for ~80% of AMD-related visual impairment. Although the current intravitreal injection of VEGF inhibitor therapy (e.g. Lucentis or Avastin) can stabilise or even improve visual function, approximately 50% of treated eyes may develop macular scar, which causes irreversible sight loss. Currently, there are no medications to prevent or treat this condition due to a lack of understanding of the disease mechanisms.

Myofibroblasts play a key role in converting the diseased blood vessels into fibro-vascular membranes in wet AMD. Myofibroblasts do not exist in the macula and currently, we do not know where they come from and how they are activated in wet AMD. Recently, a special type of cells around the blood vessels called perivascular mesenchymal stem cells (pMSC) was found as a major source of myofibroblasts in injury-induced scar formation in multiple organs, including the lung, kidney, and heart. These pMSCs are known to safeguard the blood vessels and maintain their integrity. During injury, they detach from the blood vessel wall and travel to the site of damage, where they participate in tissue repair and regeneration. When the injury persists or injury-mediated inflammation does not resolve promptly, the pMSCs expand and become myofibroblasts leading to organ fibrosis. We have found that the neuronal retina and choroid also contain a network of pMSC. We also detected a large number of pMSC that co-expressed myofibroblast markers in macular scar secondary to wet AMD. This proposal aims to understand why pMSC become scar-causing myofibroblasts in wet AMD and to work out a strategy to prevent or revert this process. We will use advanced genomic techniques to gain insight into the specific subtypes of pMSC that give rise to myofibroblasts and the pathways that control their activation and differentiation. We will then verify the pathways in vitro and in vivo and will use pharmacological approaches to prevent or revert the differentiation of pSMC into myofibroblast.

The findings of this project will advance our understanding of retinal repair and scar formation in wet AMD and other sight-threatening diseases caused by abnormal tissue repair and wound healing such as proliferative diabetic retinopathy and proliferative vitreoretinopathy. Ultimately, the knowledge will enable us to develop a method to prevent or treat retinal scar.

Grants and awards

NIHR HTA
SINFONIA: Sugammadex for prevention of post-operative pulmonary complications
PI: **Jon Silversides**
Funded value: £1,773,402

Patients who undergo major chest and abdominal surgery typically receive a neuromuscular blocking agent (NMBA) drugs as part of a general anaesthetic. These drugs temporarily paralyse skeletal muscles, including those involved in airway reflexes and breathing, to facilitate invasive ventilation and surgical access. Despite careful monitoring, and administration of a reversal agent at the end of anaesthesia, one in three patients experience residual paralysis at the end of surgery, which leaves them with weak airway and respiratory muscles, predisposing to post-operative pulmonary complications (PPCs) such as atelectasis and pneumonia which result in longer hospital stay and greater risk of death.

Two NMBA antagonist drugs are available to reverse paralysis. Neostigmine has been used since the
1950s, but can itself cause muscle weakness. Observational data suggest that sugammadex, a newer drug, may reduce PPCs by a third compared with neostigmine, but patient benefit remains unproven, and there are concerns about cost and drug allergy. In Japan, routine sugammadex use has led to a dramatic increase in life-threatening allergies.

SINFONIA is a pragmatic multi-centre randomised trial which will define the risks and benefits of sugammadex use for patients aged >=50 years undergoing major thoracic or abdominal surgery in one of 40 participating NHS hospitals. Outcomes include Days Alive and out of Hospital within 30 days after surgery (DAH30), a summary measure of recovery and survival after major surgery. Secondary outcomes
Include the rate of allergic sensitisation, PPCs, mortality, health-related quality of life and cost effectiveness. SINFONIA will define the standard of care for NMBA reversal for patients having major surgery in the NHS.

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Grants and awards

European Respiratory Society
NEw Understanding in the tReatment Of COUGH (NEUROCOUGH)
PI: Lorcan McGarvey
Co-Chairs: Professor Lorcan McGarvey (QUB); Professor Lieven Dupont (KUL)
Funded value: £577,684
Project award: 1.24 Million Euro

Chronic cough is a common and troublesome clinical problem and currently there are no effective treatments (1). While individual specialist cough clinics have been set up in some European countries there is no formal mechanism to develop common management approaches. Furthermore, the vast majority of clinical trials of novel anti-tussive treatment have been conducted in a limited number of sites in the United Kingdom and United States with little in the way of cough clinical trial infrastructure across Europe (2-7).

The **NE**w **U**nderstanding in the t**R**eatment **O**f **COUGH** (**NEuroCOUGH**) Clinical Research Collaboration seeks to create a unique platform allowing clinicians together with patients, researchers in academia and industrial partners across Europe and beyond to exchange ideas and facilitate collaborations geared towards improved care and treatment for patients with cough.

The project is a multicentre observational cohort study. Among the objectives of the study are:

- To provide a Europe-wide database of carefully phenotyped cough patients
- To provide a well characterized clinical cohort available to undertake and multi-centre clinical trials and innovative sub-studies designed to elucidate novel pathophysiological mechanisms underlying cough
- To serve as an important resource of biological samples from cough patients suitable for genetic studies and genomic and proteomic analysis
- Create a Registry of Europe-wide Specialist Cough Clinics operating according to agreed and standardised protocols.
- Establish a Europe-wide registry of 'clinical trial ready' chronic cough patients suitable for multi-centre experimental medicine studies and later phase precision medicine clinical trials.
- Provide information on the clinical pattern and healthcare burden of chronic cough in primary care by analysing the large 'real life' databases.
- Promote Education and Patient/Public Engagement in the field of cough

NEUROCOUGH will place Europe at the forefront of clinical improvements in chronic cough and provide a strong platform for attracting major clinical trials of anti-tussives, thus speeding up drug discovery with the ultimate aim of providing better treatments for patients with chronic cough.

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Grants and awards

HSC R&D
PREhabilitation for Patients Awaiting liveR transplantation: development and feasibility testing of a remote multicomponent prEhabilitation intervention: PREPARE
PI: Judy Bradley
Co-I: WalkerSuzanne Lester, Dr Bronwen Connolly, Dr Johnny Cash.
Funded value: £213,781

The liver is a vitally important organ in the body as it stores energy supplies (glycogen). In patients with end stage liver disease, the liver is damaged by inflammation and scarring ('cirrhosis'). Liver cirrhosis can lead to impairment of liver function. The liver cannot store glycogen as efficiently, which means the body needs to use other sources of energy. One of these other sources is called protein, which is mainly stored in muscles. Therefore patients with end stage liver disease often notice that they lose weight and strength from their muscles, which in turn makes them feel weaker this is known as sarcopenia. Sarcopenia in patients with end stage liver disease is very common. Presenting with sarcopenia before surgery in patients with end stage liver disease who are awaiting liver transplantation may result in poorer recovery afterwards. Interventions aimed at preventing or minimising sarcopenia could increase physical function, increase muscle strength and muscle mass, and improve patient well-being. A remote multicomponent prehabilitation intervention that aims to improve sarcopenia prior to liver transplantation has the potential to reduce overall hospital length of stay and reduce waiting list mortality whilst resulting in improved post-surgical outcomes. In this study, we will therefore explore if a remote multicomponent intervention delivered to patients with end stage liver disease whilst they are awaiting liver transplantation The project aim is to develop and test the feasibility of a remote multicomponent prehabilitation intervention for patients with end stage liver disease awaiting liver transplantation.

The overall project includes 4 studies-

Study 1- A scoping review to map and understand the evidence on prehabilitation in the major surgery population as prehabilitation in the Liver Transplantation population is a novel concept.

Study 2- Focus groups will be carried out with patients, caregivers and clinicians separately. The focus groups will explore opinions, experiences, facilitators, and barriers. They will also explore the possible content, format, components, and outcomes to include in the novel remote multicomponent prehabilitation intervention.

Study 3- Experienced based co-design workshops to collaboratively design a remote multicomponent intervention in partnership with patients awaiting liver transplantation, caregivers and clinicians.

Study 4- A single centred, non-randomised, feasibility study to test the co-designed intervention in patients with end stage liver disease awaiting liver transplantation in a single Regional Liver Unit to test the intervention. The testing will include recording its delivery, fidelity, recruitment rates, and outcomes.

In this study, we will explore if a remote multicomponent intervention delivered to patients with end stage liver disease whilst they are awaiting liver transplantation The project aim is to develop and test the feasibility of a remote multicomponent prehabilitation intervention for patients with end stage liver disease awaiting liver transplantation.

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Students raise £1,491 for MS Research at Queen's

Earlier this year Primary 7 pupils Fionn and Callum from St. Joseph's Primary School, Downpatrick raised £1,491 from their sponsored walk in Delamont Country Park for MS research at Queen's. Pictured are Fionn and Callum presenting a cheque to Development Manager Stephen O'Reilly.

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