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Professor José Bengoechea
WWIEM Director

Welcome

With the Institute, as the rest of the country, in lockdown since 23rd March under the current COVID-19 crisis, we are living an unprecedented situation that has changed and will continue to change the way we work and live. Our staff wellbeing is our priority, that is why we recommend you to stay home, stay safe, and work from home until new guidelines are disclosed. Please do check the FAQs of the University to get updates on how the University is adapting its operations during COVID-19. It is important to keep connected, and support our colleagues specially those more affected by the lockdown, namely 3rd year PhD students, and postdocs and technicians working in projects ending during 2020.

I want to thank the superb work of our professional services to secure continuity of our work.

The clerical team has ensured a smooth working from home operations including the assessment of our PhD students. operations and supporting on-going COVID-19 research. The technical team is providing support on site to other parts of the health campus by operating stores, contributing to the tests efforts of the NHS, while maintaining WWIEM essential work.

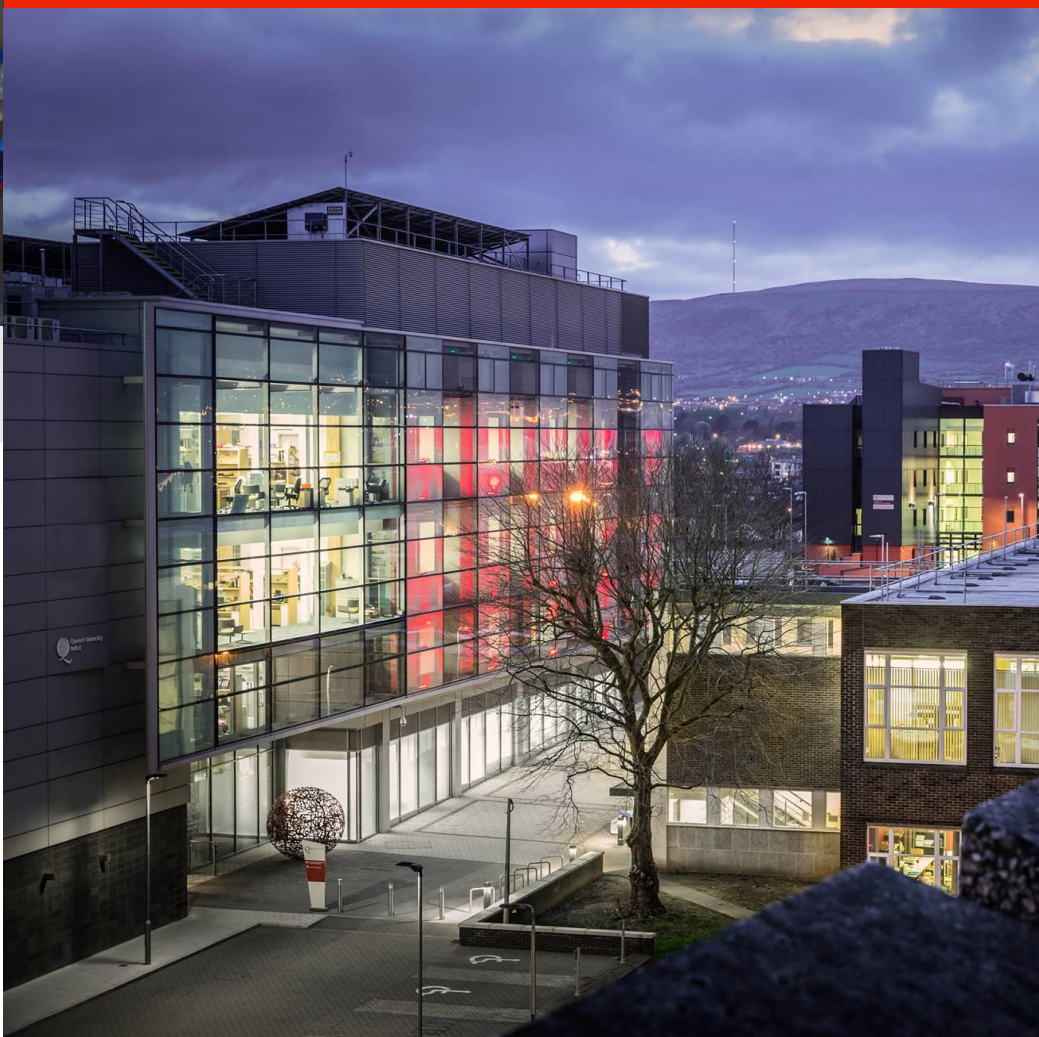
I am particularly proud of WWIEM contribution to research on COVID-19, leading some of the most innovative studies, including pioneering clinical trials, to find new treatments to treat COVID-19 patients. In addition, I want to acknowledge the work of our clinical colleagues at the front line of the NHS to treat COVID-19 patients.

We are now working to establish a safe way of returning to work as soon as the NI Executive and the University understand it is appropriate. The situation is fluid but we are getting ready to return to work as soon as we possibly can. Our return to work, however, will not be a return to our usual way of working. Social distancing, and strict health and safety measures, in the interest of all, will be in place following the guidelines established by the University. With your help, and working as a team, I am confident we will be able to re-establish our research programmes to tackle major health issues in addition to COVID-19.



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Meet our Researchers



**Dr Guilherme
Costa**

Guilherme joined WWIEM in late 2019 as Lecturer, from the University of Manchester, where he received a PhD in 2011 for his studies on embryonic haematopoiesis. He moved on to a postdoctoral position and in 2017 he was awarded the Dean's Prize: Early Career Researcher Award from the University of Manchester. With this award, he initiated an independent research career focusing on the spatial regulation of gene expression in the context of endothelial biology. At the WWIEM, he will set up a research programme to investigate how RNAs are transported in endothelial cells, how protein synthesis is regulated within subcellular domains and how these mechanisms regulate blood vessel development and function. Ultimately, these studies will contribute to further understanding complex biological processes underpinning blood vessel formation, maintenance and pathology.



**Dr Eleni
Beli**

Eleni is a Vice Chancellor fellow who joined WWIEM in August 2019, after a postdoctoral research period at Indiana University School of Medicine. With a focus on diabetic complications, she is investigating how a desynchronized biological clock in diabetes affects progression of diabetic retinopathy. Currently, her focus is on how to align these broken diabetic cellular rhythms with different feeding regimens in order to prevent diabetic retinopathy. Her laboratory is interested in chronotiming drug delivery, biomarker sampling and in designing non invasive lifestyle interventions to delay the onset of diabetic retinopathy. She is focused in studying physiological and systemic parameters affecting innate immunity and retinal health. Her lab uses type 1 and type 2 diabetic models and multi-omics approaches to identify metabolic and microbial derived signatures that affect innate immune cell function and vascular health.



**Dr Bianca
Plouffe**

Bianca is a Vice-Chancellor's Fellow, who joined WWIEM in November 2018, from a position as Postdoctoral researcher at the Institute of Research in Immunology and Cancer (University of Montreal) and got her PhD from University of Ottawa. She is establishing her research programme in the area of G protein-coupled receptors (GPCRs), which are the targets of about 33% of actual pharmacological treatments. GPCRs activate G proteins regulating many signalling events, and was originally believed to be restricted to plasma membrane. However, recent advances in spatial resolution of subcellular events demonstrate that some GPCRs also activate G proteins into intracellular compartments resulting in unique spatiotemporal signalling properties. Bianca aims to tackle key mechanistic questions underlying this non-canonical signalling and to exploit it to target type 2 diabetes, glioblastoma multiforme, and atherosclerosis.



**Dr Dessi
Malinova**

Dessi is an immunologist and cell biologist interested in the molecular mechanisms of immune cell function. She completed her PhD in Molecular Immunology at UCL Great Ormond Street Institute of Child Health in 2014. This focused on elucidating how immune cells interact and communicate directly to mount an effective immune response. She joined the MRC National Institute for Medical Research/ Francis Crick Institute as a postdoctoral researcher, where she continued to study adaptive immunity, particularly B cell activation and antibody responses. This led to the characterisation of novel endocytic pathways for antigen-triggered B cell receptor. Dessi joined WWIEM in 2020 as a Patrick G Johnston Fellow to establish her independent research in immune cell receptor activation in health and disease.

Awards, Prizes and distinctions



Professor Ultan Power

Professor Ultan Power joins expert advisory group feeding into SAGE

Prof Ultan Power was invited by the Academy of Medical Sciences and the British Society of Immunology to join in April an expert group to collate what is currently known about the immunology of COVID-19 and develop Immunology research priorities in response to the coronavirus outbreak (COVID-19).

On 1 May 2020, the expert group published a rapid review of the relevant immunology research to help us understand how it can inform our response to the COVID-19 pandemic, and the key research priorities for COVID-19 immunology research.

Professor Stuart Elborn elected Fellow of The Academy of Medical Sciences

Professor Stuart Elborn, is among 50 of the UK's most prominent biomedical and health scientists elected to The Academy of Medical Sciences' Fellowship. The new Fellows were chosen for their exceptional contributions to advancing biomedical science via world-leading research discoveries, running national science communication and engagement programmes and translating scientific advances into benefits for patients and the public. The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. The new Fellows will be formally admitted to the Academy on 25 June 2020.



Professor Jose Bengoechea

Prof Jose Bengoechea, new member of MRC's Infection and Immunity Board

Professor Jose Bengoechea joined in January 2020 the MRC's Infection and Immunity Board (IIB). The IIB is responsible for the MRC's investments in infectious human disease and disorders of the human immune system. IIB is providing strategic direction to enable the best research possible. IIB not only allocates the funding for investigator-led grants within its area of remit, but also manages a range of strategic investments and partnerships. He is also, since 2019, a core member of BBSRC committee D, after being panel member of this committee since 2013.

Professor David Grieve, Vice-chair of the BHF Project Grants Committee

Professor Grieve has been designated Vice Chair of the British Heart Foundation Projects Grants Committee, after serving as panel member since 2017. He will continue in this role until February 2021.

Professor Tim Curtis, Co-Lead in the Physiology Society

Professor Tim Curtis is Co-lead of the Vascular and Smooth Muscle Theme for the Physiological society.

Dr Fionnuala Lundy, new President for the International Association for Dental Research

Dr Fionnuala Lundy has been announced as President Elect for the Pan-European region of the International Association for Dental Research 2019-2020, taking over as President of the Pan-European region in Sept 2020.

Alérie Guzman de la Fuente to attend the Lindau Nobel Laureate Meeting

Alérie Guzman de la Fuente has been accepted as a young researcher for the Lindau Nobel Laureate meeting in June. Only 650 applicants are given the opportunity to attend the Lindau Nobel Laureate Meetings.

Development weeks

A new edition of Development weeks took place in January 8th. The following groups helped host our Year 1 BSc students for their Development Week activity. The feedback was excellent and they really appreciated hearing about the research from the PhD students and Postdocs.

Station 1: Grieve/Watson

Station 2: Lengyel

Station 3: Krasnodembskaya

Station 4: Margariti

Station 5: Bengoechea and Schroeder

Development weeks provide students with dedicated time and space to take part in extra-curricular activity and gain Degree Plus accreditation. Introduced in 2016/7 as part of the Academic Year restructuring, development weeks aim to complement learning and development within each students degree programme, provide students with opportunities to gain skills beyond their degree pathway, engage with staff and students across the university, offer students the chance to realise their ideas in a supported and low risk environment and provide an opportunity for experimentation and innovation outside of the curriculum.



Annual Postdoc Symposium 2020

The 4th Annual WWIEM Postdoctoral Research Symposium took place on the 24th January 2020 in WWIEM. The event has gotten better each year and there was a great buzz throughout the day.

Professor Jose Bengoechea opened the symposium and Professor Denise Fitzgerald contributed with the closing remarks.

Congratulations to Amy Dumigan and Andrew Young for 1st and second prizes for best oral presentations and Flavia Viani and Anna Claire Devlin for the best posters.

Congratulations to Lauren Kerrigan for the poster networking prize and Joana Sa Pessoa for winning the imaging competition.

Special thank you to the PCDC organising committee: Maria Llorian Salvador, Amy Dumigan, Ryan Brown and Judith Lechner.



Outreach

Northern Ireland Science Festival

WWIEM offered its annual Open Day Science Event as part of the NI Science Festival on 15th February.

The Institute hosted a sold out event for the NI Science Festival, Lab View 360: Biomedical Research in Action. In a change to the format of previous years, Visitors became a scientist for the afternoon and went on structured lab tours in WWIEM. Through a range of demonstrations and interactive laboratory research activities across three disease areas; eye disease, diabetes/vascular disease, respiratory/infectious disease, the Visitors got a view of working research labs in action.



COVID-19 Research response from WWIEM

Since the start of the COVID-19 crisis in the UK, WWIEM researchers have been extremely responsive.

PI's at WWIEM are leveraging our internationally recognized expertise in viral infections, diagnosis of infections, and clinical trials to lead the research response to COVID-19.

UKRI rapid research response fund for novel coronavirus research

UKRI funded; Ultan Power and Ken Mills

Professor Ultan Power and Professor Ken Mills (CCRCB) will test a library of approximately 1,000 drugs on cells in the laboratory to determine if any can reduce the toxic effects of novel coronavirus infection. The drugs are already approved for use in humans. They will be tested on airway epithelial cells grown in the lab and infected with novel coronavirus to determine if the drugs can reduce virus infection or replication and virus-induced inflammatory responses. This could identify promising drugs for further testing and clinical trials in 12 months.

COVID-19 Genomics UK (COG-UK) Consortium

UK Government; David Simpson & Derek Fairley (BHSCT)

WWIEM's David Simpson is working as part of the COVID-19 Genomics UK Consortium (COG-UK) which has been created to deliver large-scale and rapid whole-genome virus sequencing to local NHS centres and the UK government. Its data will help Public Health Agencies to manage the COVID-19 outbreak in the UK and inform vaccine research efforts.

Belfast is one of a network of centres throughout the UK which will sequence samples from local confirmed cases of COVID-19. The goal of the COG-UK Consortium is to deliver large-scale SARS-CoV-2 genome sequencing capacity to hospitals, regional NHS centres and the Government that, when combined with epidemiological and clinical information, will inform interventions and policy decisions during the current UK COVID-19 epidemic. The COG-UK Consortium is an innovative partnership of NHS organisations, the four Public Health Agencies of the UK, the Wellcome Sanger Institute and more than 12 academic institutions providing sequencing and analysis capacity. It is supported by £20 million funding from the UK Department of Health and Social Care (DHSC), UK Research and Innovation (UKRI) and the Wellcome Trust.

Development of a COVID-19 rapid diagnostic test.

H2020 - EU funded; Cliff Taggart

Professor Cliff Taggart, in partnership with HiberGene Diagnostics Ltd, Medcaptain in China, and Italian Hospital IRCCS Ospedale Policlinico San Martino, have been awarded support from EU H2020 to develop a highly accurate diagnostic test for COVID-19 that aims to show results within an hour. The test would enable clinicians to test for COVID-19 on site, eliminating the need to send tests to a centralised laboratory.

Seroprevalence of SARS-Cov-2 Antibodies in Children

Public Health England commissioned; Thomas Waterfield & Chris Watson

Thomas Waterfield and Chris Watson are conducting a study, in collaboration with Public Health England, to investigate the seroprevalence of SARS-Cov-2 antibodies in children. Four sites across the UK (Belfast, Glasgow, London and Manchester) will recruit 800 children. Immunoglobulins M and G to SARS-Cov-2 will be measured at baseline, eight weeks and six months.

COVID19 Research response from WWIEM

Clinical trials

Recovery –RS. UK-wide clinical trial to treat hospitalised patients with COVID-19

NIHR funded; Danny McAuley, Judy Bradley, Bronwen Connolly

This new clinical trial led by the University of Warwick seeks to find alternatives to ventilators to treat patients who are critically ill with COVID-19. The project is testing the efficacy of non-invasive interventions at an earlier stage in disease progression as an effective alternative to using ventilators for COVID-19 patients.

The RECOVERY-RS Respiratory Support trial will recruit 4,000 patients with the aim to find effective alternative solutions for patients with COVID-19; to reduce the need for treatment with a ventilator and to improve patient outcomes.

The study is based on the theory that non-invasive interventions at an earlier stage may reduce the need for invasive ventilation with a mechanical ventilator.

The trial will enable researchers to see whether any of the possible new treatments are more or less effective than those currently used for patients with COVID-19.

UK-wide cell therapy clinical trial for COVID-19 patients with acute respiratory failure

HSC funded; Cecilia O’Kane & Danny McAuley

As part of the UK response to the COVID-19 pandemic, the Wellcome Trust funded REALIST clinical trial is assessing a novel allogeneic stromal cell therapy in a Phase 2 trial targeting Acute Respiratory Distress Syndrome (ARDS) caused by COVID19.

Recent reports indicate that 80-90% of COVID19-related deaths are caused by ARDS and ICU patients with moderate-severe ARDS caused by COVID19 have a 28-day mortality rate of ~50%.

There are currently a significant number of vaccines and therapies in development for targeting the SARS-CoV-2 infection. All of these treatments are targeting the virus and its ability to infect and replicate within the body. However, few therapies are in development to address ARDS.

REALIST is a 1:1 randomised, Phase 2, placebo-controlled, double blind study assessing the ORBCEL-C stromal cell immunotherapy in 60 patients with moderate-severe ARDS caused by COVID19. The REALIST open label Phase 1 safety trial was successfully completed in 2019.

The REALIST trial is led by Professor Danny McAuley and Professor Cecilia O’Kane at Queens University Belfast and was approved and listed by UK NIHR as an Urgent Public Health Research Study. REALIST is already enrolling patients and plans to recruit at least 60 patients throughout the Covid-19 pandemic at multiple sites across the UK, including Belfast, Birmingham and London.

Does treatment with hypertonic saline and/or carbocisteine decrease sputum viscosity, elasticity, inflammation and bacterial load in the lungs of patients with bronchiectasis?

Efficacy and Mechanism Evaluation –EME

MRC- NIHR

Cliff Taggart; Judy Bradley, Danny McAuley, Stuart Elborn, Michael Tunney (Pharmacy) and Mike Clark (CPH)

This project is the first EME award that WWIEM, and Queen's, have received from this programme, making Professor Taggart's achievement a brilliant milestone.

The Efficacy and Mechanism Evaluation (EME) is a partnership between the Medical Research Council (MRC) and the NIHR. The programme funds ambitious studies evaluating interventions with potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies, EME supports research in the mechanisms of diseases and treatments.

The EME Programme looks to attract studies with novel methodological designs that deliver results more efficiently, reduce the study timeline, and maximise the knowledge gained. The translational research it supports covers a wide range of new and repurposed interventions, such as diagnostic or prognostic tests and decision-making tools, therapeutics or psychological treatments, medical devices, and public health initiatives delivered in the NHS.

The project focuses in treatment for patients with bronchiectasis. They experience frequent exacerbations, which can cause irreversible damage to lung tissue and reduce lung function. Treatment with hypertonic saline reduces the frequency of exacerbations and improves lung function in patients with Cystic Fibrosis. Carbocisteine reduces pulmonary exacerbations in patients with COPD and significantly reduces levels of the inflammatory mediators, interleukin-6 and 8-isoprostane. Other mucoactive drugs have been shown to reduce the viscosity of sputum in patients with CF and asthma, which suggests that a reduction in sputum viscoelasticity may be a mechanism by which these drugs reduce inflammation, improve lung function and reduce exacerbations in chronic lung disease.

The use of hypertonic saline and carbocisteine are being evaluated in patients with bronchiectasis as part of the CLEAR trial. CLEAR is a 2x2 factorial randomised open label trial to determine the clinical and cost- effectiveness of hypertonic saline and carbocisteine versus usual care to reduce exacerbations in bronchiectasis. In bronchiectasis, highly viscoelastic airway secretions are partially responsible for the pulmonary manifestations of bronchiectasis. In this study, we will assess sputum samples obtained from the CLEAR trial to determine if reduction in sputum viscosity and elasticity can explain any decreases in pulmonary exacerbations observed as part of the CLEAR trial in patients treated with hypertonic saline, carbocisteine or both.

In addition, we will also measure sputum mediators such as IL-6, 8-isoprostane and IL-8 all known to be increased in bronchiectasis to see if hypertonic saline and carbocisteine treatment can also reduce inflammation in these patients. Finally, the impact of hypertonic saline and carbocisteine on bacterial load in sputum will also be assessed in these sputum samples as reductions in exacerbation may be associated with decreases in bacterial burden.

Academy of Medical Sciences Springboard awardees

Springboard. AMS.

Rebecca Coll. Effie Kostareli

Rebecca Coll and Effie Kostareli were awarded the Academy of Medical Sciences Springboard, round 5. The award provides £100,000 over two years and a personalised package of career support to help newly independent biomedical scientists to launch their research careers.

Dr Rebecca Coll. “Investigating the regulation of the human NLRP3 inflammasome”.

The aim of this project is to understand how a type of white blood cell called a macrophage causes inflammation. Inflammation is generally beneficial to us. For example, when we get a cut on our finger, the redness and pain that we feel actually helps us clear the infection and heal the wound. However, there are many diseases including arthritis, liver disease, and Alzheimer’s disease, where immune cells like macrophages cause damaging inflammation. Previous research has shown that a protein called NLRP3 causes this type of damaging inflammation, and that drugs which block NLRP3 activation could be used to treat these diseases. I want to understand more about how NLRP3 is activated. My initial experiments show that blocking another type of protein called PI3K can indirectly make NLRP3 hyperactive, causing excessive inflammation, but this only happens in human cells and not mouse cells (which we usually use to study NLRP3). I want to use a new model of human macrophage cells made from induced pluripotent stem cells (iMacs), in order to examine this PI3K-NLRP3 connection. I will use the iMacs in combination with gene editing technology to make small changes in NLRP3 to see how this affects its activation. PI3K is part of a network of proteins so I will also use drugs that block parts of this network to map how PI3K connects to NLRP3. Ultimately, though understanding more about NLRP3 activation in human cells, this may help the development of new drugs for people suffering with inflammatory diseases.

Dr Effie Kostareli. “Epigenetic effects of BTK inhibition in chronic lymphocytic leukaemia”.

In Chronic Lymphocytic Leukaemia-(CLL), the treatment paradigm has shifted from nonspecific chemoimmunotherapy to B-cell-receptor inhibitory (BCRi) therapies. Ibrutinib-(Ib), an inhibitor of Bruton tyrosine kinase-(BTK), has been at the forefront of the paradigm shift. Although Ib is viewed as a revolutionary treatment for CLL, providing results never seen before, Ib-resistance occurs especially in patients that are difficult to treat. It is therefore an imperative need not only to thoroughly understand BTKi-resistance mechanisms, but also to discover biomarkers for stratification of patients who require tailored alternative treatments. This proposal aims at bridging the knowledge gap between BTK-signalling and epigenomics and thereby contributing to shaping concepts in the emerging field of pharmaco-epigenomics. Our mission is to offer compelling insights into BTKi-resistance and discover novel biomarkers for precise treatment algorithms which are urgently needed. We will address this challenge by using a combination of robust epigenetic analyses and finely-tuned molecular experiments. This proposal will offer novel fundamental knowledge for BTK-epigenomics, which is critical in order to tackle the problem of BTKi-resistance, especially now with the approval of Ib as a first-line therapy. The highly innovative nature of the project emerges from the unique opportunity to combine state-of-the art epigenetic research with a robust clinical model and a pharmacological-relevant pathway. Moreover, Ib-cost-effectiveness issues for NHS along with the lack of consensus in treatment algorithms worldwide make imperative the need not only for unravelling BTKi-resistance mechanisms but also for identifying smart biomarkers which will allow us to shift towards a precision medicine model for CLL.

Other Grants and awards

“Targeting the compromised brain endothelial barrier function during cerebral malaria with AT2 receptor agonists”

US-Ireland R&D partnership programme. Alan Stitt

Led by University College Cork, the project aims to identify a lead compound, which can stimulate specific intracellular signalling through the AT2 receptor to mediate essential protection of endothelial integrity during cerebral malaria to prevent this life-threatening pathology. Reinforcement of a functional cell barrier through the modulation of specific receptors may even prove to be a key target for prevention and treatment of other hemorrhagic diseases affecting other organs, such as viral hemorrhagic fevers (Ebola) or acute respiratory distress syndrome caused e.g. by the Covid-19.



Help support the pursuit of world-class education and life-changing research

If you would like to donate to any of the research programmes within WWIEM, please contact **Sarah-Jayne Cassells**, Development Manager (Health), Queen's University Belfast; Tel: (+44) 028 9097 5073; Email: S.Cassells@qub.ac.uk. Alternatively, go to **Queen's Foundation - Donate Now** @ <https://daro.qub.ac.uk/DonateNow>. Within the donation form, you can specify how you would like your gift to be used.

Queen's Foundation have launched a new online fundraising guide for people who would like to raise money directly for WWIEM. The simple guide provides helpful tips on planning and promoting a fundraising event, using JustGiving and it includes poster / flyer templates and a sponsorship form. Check it out online at @ https://daro.qub.ac.uk/file/QUB_fundraising_Guide.pdf or contact Sarah-Jayne Cassells for more information.

