



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

Annual Overview of Doctoral Health Research 2022

School of Medicine





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Clinical Medicine - TB immunology 45

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Clinical Medicine 45

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PhD	Investigating the impact of immune senescence in Age-related Macular Degeneration	45
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PhD	Iron and its Ferocious role in alveolar type II epithelial cell dysfunction in chronic lung diseases	45

PhD	Defining the role of Th17 lineage cells in human pulmonary health and disease	45
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MD	Outcomes of Paediatric Inclusion Health	45
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MD	HDL cholesterol efflux capacity (HDL-CEC), HDL lipoprotein function and lipidomic analysis in T1DM and risk of atherosclerosis	45
MD	Prevalence of and Interventions for Fatigue in Patients with Inflammatory Bowel Disease	45
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MD	An Evaluation of Epilepsy and Driving in Ireland including Patient Impact, Understanding among Healthcare Professionals, and Digital Resource Development	45

Clinical Microbiology 45

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PhD	Antisocial Behaviour in the Cystic Fibrosis Airway Microbiome	45
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PhD	Investigation of Molluscum Contagiosum Virus inhibitor MC089 which targets IRF activation	45
PhD	Investigation of Molluscum Contagiosum Virus inhibitor MC008 which targets human DNA sensing.	45
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PhD	Phenotype and Function of Neutrophil subtypes in ANCA vasculitis	46
PhD	Cross- Disease Assessment of Phenotypic and Functional Granulocyte Heterogeneity	46
PhD	VAPRE: Exploring the Relapse Prodrome of ANCA associated Vasculitis	46

Gastroenterology 46

MD	A study of clinical scores, investigation and management of gastrointestinal bleeding	46
MD	An investigation of completion rates in capsule endoscopy	46

Haematology 46

MD	Determinants of Immune Reconstitution After Allogeneic Haematopoietic Stem Cell Transplantation Performed With Anti-T-Lymphocyte Globulin	46
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Medical Gerontology 46

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PhD	Clinical Decision Support Combining Cerebral Perfusion and Machine learning in Falls and Syncope Management	46
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PhD	An Investigation of Physical Activity, Physical Health and Clinical Bleeding Phenotype in Adults with Moderate and Severe Haemophilia in Ireland.	49
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PhD IMPORT- Interactive monitoring of paediatric outcomes for radio and chemo therapies	50
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PhD Effect of radiation in visceral adipose tissue in Oesophageal Cancer patients	50
PhD Boosting oxygen diffusion in the radioresistant Oesophageal tumour microenvironment to improve radiation response.	50
PhD Immunophenotyping of pancreatic cystic lesions	50
PhD Enhancing immunotherapy in Oesophageal Adenocarcinoma through the modulation of immunometabolism with novel small molecule inhibitors Quininib and its analogues	50
PhD Harnessing the power of the immune system to fight obesity-associated cancer	50
PhD Therapeutically remodelling the immune profile of 'cold' tumours in obesity-associated cancer.	50
PhD Investigation of the role of miRNA in the treatment resistance of gastro-oesophageal cancer	50
PhD Targeting metabolism for individualised rectal cancer treatment	50
PhD Investigation of the role of the complement system in treatment resistance of rectal cancer	50
PhD Role of miR-31 in modulating chemoradiosensitivity in pancreatic adenocarcinoma	50
PhD Multi-omics in stratifying risk in patients with pancreatic intraductal papillary mucinous neoplasms	50
PhD Developing and Feasibility Testing of a Pragmatic, Patient-Centred Exercise Intervention During Chemotherapy: A Mixed-Methods Approach	50
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Foreword by Director of Research

The School of Medicine is a research-led school with strong clinical-scientific academic partnerships, based largely on the hard work of our postgraduate students undertaking PhD and MD programmes that drive excellence in research in the School.

However, the research is not sequestered in one bench, or even one laboratory, rather it is a complex collaboration between students and supervisors, across the entire campus, including early career and established scientists and clinicians. While postgraduate research is exciting and often fulfilling, even in the best of times it can be demanding. In the last two years throughout the global pandemic there were a great many more challenges faced by our postgraduate students, and I could not be prouder of how they have risen to these challenges with resilience and determination stimulated by a passion for creative learning. The research in the School of Medicine is embedded in clinical translation which inspires our postgraduate students to enhance our understanding of science and technology to the ultimate benefit of patients and professionals in the broader health system and the whole of society in Ireland.

As Director of Research for the School of Medicine I never cease to be amazed and I am extremely proud of the breadth and depth of excellence in research currently being undertaken by our postgraduate students and their supervisors in the School, as highlighted in this brochure. Indeed, our postgraduate students are involved in inspiring research spanning a wide variety of disciplines including but not exclusively cancer, infection/immunology, childhood health, neuroscience/immunology population health/health policy and ageing. The multidisciplinary and collaborative nature of the research between scientists and clinicians in the School of Medicine may start with our postgraduate students but often leads to advances in basic science and translational research. Advances that shape

our understanding of health and disease across the spectrum of disciplines at every stage of life with the potential to impact not only on today's patients but those of future generations.

In conclusion, while postgraduate research may be very rewarding, it can be frustrating, in that positive results are not always obtained, however it is important that our students realise the integrity of the process and the importance of the null hypothesis in informing our knowledge too. To complete their postgraduate programme, our students need to be inquisitive, highly motivated, skilled in communication/presentation and develop an ability to multitask, but above all they need to possess a drive and a passion for their research. In addition, they need to enjoy their work, so a little fun and laughter with support from their supervisor and the research team on the difficult days does help.

I am confident that in the current cohort of postgraduate students, we have future leaders in clinical and translational research who will have a significant impact on the health of our nation.



Prof Ursula Fearon

Foreword by Director of Postgraduate Learning and Teaching

Postgraduate research is demanding and it takes place over a long period of time. It can also be wonderfully satisfying and intellectually stimulating. The research contained in this booklet showcases just some of our most recent postgraduate researchers from within our School.

We have representation from MSc., Ph.D., and M.D. student projects. I am humbled by some of the areas of focus, the passion for research and the ambitious research questions that are clearly articulated within these pages. Areas such as health inequalities, innate immune training, sedentary behaviour, cancer treatments, and nanomedicine are just some of the exciting topic areas under investigation.

Students will have their own motivations as to why they have decided to pursue a postgraduate degree by research. Some may be motivated by a genuine curiosity to learn more, to grow or to help to solve some of today's most 'wicked problems'. Others may focus on additional skills, qualifications and potential employability after their research is completed and their degree awarded. Most students have a combination of all of these motivational factors. This is a good thing, as it will foster resilience to push through the challenges that they will face in completing their research. Whether that be recruitment of participants, delays with vital supply

chains, or even periods of doubt. Some of our students balance their research with clinical commitments, some are parents to young children, some provide care to ageing parents, some are new to Trinity and new to Ireland, some are graduates of ours and grew up locally, some are re-entering education after a long time working professionally. We pride ourselves in terms of diversity and inclusivity within our School.

Hard work is required to complete a postgraduate degree, but this is not done in isolation. Supervisor/s, and indeed the School is a supportive environment for postgraduate research. We want to build on this and help students to grow in competence and confidence. In this way, we can do our part in training, educating and preparing some of the best scientists, researchers and academic clinicians that Ireland has ever seen.



Professor Catherine Darker

School of Medicine Academic Doctoral Mentors and Supervisors

Anatomy

Denis S. Barry, Assistant Professor

Clinical Medicine

Adriele Prina-Mello, Assistant Professor

Patrick Walsh, Associate Professor, Clinical Medicine

Joseph Keane, Clinical Professor

Alan Irvine, Professor of Dermatology

Clíona Ní Cheallaigh, Associate Professor Consultant

Ignacio Martín-Loeches, Clinical Senior Lecturer

Maria O'Sullivan, Associate Professor in Human Nutrition

Sarah L. Doyle , Associate Professor in Immunology

Sharee Basdeo, Research Assistant Professor

Suzanne Cloonan, Assoc Professor In Respiratory Biochemistry

Microbiology

Julie Renwick, Assistant Professor

Stephen G.J. Smith , Associate Professor

Johannes Wagener, Associate Professor Consultant

Tom Rogers, Adjunct Professor

Clinical Medicine

Gareth Brady , Assistant Professor

Mark Alan Little , Professor Consultant

Health Policy & Management

Steve Thomas, Edward Kennedy Chair of Health Policy and Management

Charles Normand, Adjunct Professor

Peter May , Research Assistant Professor

Immunology

Derek Doherty, Professor in Immunology

Niall P. Conlon , Clinical Professor

David Edgar , Clinical Associate Professor

Medical Gerontology

Cathal McCrory, Associate Professor in Life Course Development and Ageing

Daniel Ryan, Clinical Senior Lecturer in Medical Gerontology and Consultant , Physician

Nollaig M. Bourke, Ussher Assistant Professor in Inflammageing

Román Romero-Ortuño, Professor in Medical Gerontology and Consultant Physician

Rose Anne Kenny, Regius Professor of Physic, Professor of Medical Gerontology , and Consultant Physician

Seán Kennelly, Clinical Associate Professor and Consultant Physician

Joseph Harbison, Associate Professor in Medical Gerontology and Consultant , Physician

Kevin McCarroll, Clinical Senior Lecturer in Medical Gerontology and Consultant , Physician

Molecular Rheumatology

Ursula Fearon, Professor of Molecular Rheumatology

Viviana Marzaioli, Research Assistant Professor

Neurology

Bahman Nasserolelami, Assistant Professor

Colin Doherty , Professor Consultant

Deirdre Murray , Assistant Professor and Clinical Specialist Physiotherapist

Niall P. Pender, Associate Professor in Neuropsychology

Orla Hardiman , Professor Consultant

Peter Bede, Professor in Neurology

Occupational Therapy

Deirdre Connolly , Professor in

Clodagh Nolan , Assistant Professor

Geraldine Foley , Assistant Professor

Michelle Spirtos , Assistant Professor

Tadhg Stapleton, Assistant Professor

Paediatrics

Eleanor Molloy, Professor Consultant

Pharmacology & Therapeutics

Michael Barry, Associate Professor

James Paul Spiers, Associate Professor

Laura McCullagh , Clinical Senior Lecturer

Margaret B. Lucitt , Assistant Professor

Physiology

Aine Kelly, Professor

Eric J. Downer , Assistant Professor

Eva Jimenez-Mateos , Assistant Professor

Kumlesh Kumar Dev , Professor

Maeve Caldwell, Professor in Neuroscience

Melissa J. Conroy, Senior Research Fellow

Marie-Victoire Guillot-Sestier , Assistant Professor,

Mark Oliver Cunningham, Professor of Neurophysiology of Epilepsy

Mikel Egaña , Associate Professor

Tamara Boto, Assistant Professor

Psychiatry

Declan M. McLoughlin , Professor of

Aiden Corvin , Professor Consultant

Brendan Kelly, Professor Consultant

Elizabeth A. Heron , Assistant Professor

Jane McGrath, Associate Professor Consultant

Louise Gallagher , Professor Consultant

Shigeki Nakagome , Assistant Professor

Simon McCarthy-Jones, Associate Professor

Public Health & Primary Care

Catherine D. Darker, Associate Professor

Lina Zgaga, Associate Professor

Radiation Therapy

Laure Marignol , Associate Professor

Michelle Leech , Associate Professor

Surgery

Jacintha N. O'Sullivan, Professor in

Joanne Lysaght , Associate Professor

Kevin Christopher P. Conlon , Professor Consultant

Melissa J. Conroy, Senior Research Fellow

Niamh Lynam-Lennon , Research Assistant Professor

Stephen G. Maher , Associate Professor

A Selection of Current Doctoral Research Projects in 2022

Supporting physical function in community-dwelling older adults – a focus on health inequalities and underserved groups

PhD Student: Lauren Swan

Supervisor: Associate Professor Maria O’Sullivan

Funder: North Dublin Home Care

Overview of Project:

Lauren is interested in older adult populations who are often underrepresented in traditional health research. This includes older people living with socioeconomic disadvantage, greater physical dependency, frailty, or more advanced age. Her research focuses on sarcopenia, a condition affecting muscle strength, which has been linked with adverse health outcomes. Using two large international datasets, current work suggests sarcopenia risk is significantly higher in older adults with socioeconomic disadvantage. She is also investigating the delivery of an innovative home-based physical activity programme with frail older adults. She is conducting fieldwork examining sarcopenia, frailty, nutritional status, and physical activity in older adults living in areas with socioeconomic disadvantage. This offers real-world insight into engaging and including underserved groups in health research and will inform strategies to better support ageing in place.

Long-term impact of project:

The delivery of a home-based physical activity programme with frail older adults will inform future healthy ageing initiatives aiming to translate proactive approaches into practice, as well as adding to the evidence base for inclusive strategies which address sarcopenia, promote quality of life, and support ageing in place for older citizens.

PhD Candidate Quote :

“It is hoped that my research findings will inform future studies aiming to engage and include older adult populations currently underserved in traditional health research.”



Defining the consequences of innate immune training on protective versus pathogenic T cell responses in patients with tuberculosis

PhD Student: Dearbhla Murphy

Supervisor: Dr Sharee Basdeo

Funding: Health Research Board Emerging Investigator Award (Dr Sharee Basdeo)

Overview of Project:

This research focuses on how our immune system interacts with *Mycobacterium tuberculosis* (Mtb), the bacteria that causes Tuberculosis (TB). Dearbhla focuses on how both our innate and adaptive immune system fight Mtb and how that might be used to our advantage. In the past few years there has been a rise in the number of drug-resistant TB cases, meaning the current drugs we have to fight TB do not work against the bacteria. Host-directed therapies aim to boost a patient's own immune response to help eliminate the bacteria in conjunction with antibiotics. Dearbhla is interested in using a form of immune 'training' which boosts our innate immune system, improving its ability to eliminate Mtb right after exposure to the bacteria before it causes disease. TB is a very complex disease, where the immune response acts like a double-edged sword – too little inflammation means you won't eliminate the bacteria but too much inflammation results in damage to the lungs. As such, she is also interested in better understanding the bidirectional interactions between these early 'trained' innate immune responses and longer-term immune responses with the aim that this work may inform the design of new host-directed therapies and vaccines against TB.

Long-term impact of Project:

As well as potentially forming new host-directed therapies for TB, a better understanding of the fundamentals of the human immune response will also inform diverse areas of medicine that are impacted by altered immune function, such as cancer and autoimmune diseases.

Quote:

"I hope that my work will have the potential to inform the design of new host-directed therapies or vaccines, not only for TB but for other emerging infections and drug-resistant infections."



Cross-Disease Assessment of Phenotypic and Functional Granulocyte Heterogeneity

PhD Student: Amrita Dwivedi

Supervisor: Professor Mark Little

Funding: Irish Research Council

Overview of Project:

Neutrophils are the most abundant immune cells in our body and play an important role in defence against infections and other threats. Defects in neutrophil function can have severe consequences and lead to various diseases. One such disease is Anti-Neutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis (AAV), also known as small vessel vasculitis. There are two types of small vessel vasculitis: Wegener's Granulomatosis (GPA) and Microscopic polyangiitis (MPA). Both types are characterised by antibodies that target the body's own neutrophil proteins causing defective neutrophil function. AAV is a rare disease, but can result in organ damage and failure, with the kidney and lung as major targets. As many as a quarter of AAV patients who require renal replacement therapy (kidney dialysis) at the time of diagnosis die within six months of diagnosis, and one in three patients never regain kidney function. Neutrophils were traditionally thought to be a uniform cell type with a well-defined role in the immune system, however, it is now thought that neutrophils are made up of several subclasses with specialised function which either resolve or worsen inflammation. Researchers at The Trinity Health Kidney Centre, based in the Trinity Translational Medicine Institute in Trinity College Dublin have previously shown that, in addition to normal neutrophils, a subclass of neutrophils (called 'low density granulocytes/



neutrophils') is increased in patients with AAV and is related to how severe the disease is. However, they do yet not understand whether these low-density neutrophils are directly causing AAV or whether they increase in response to inflammation. Interestingly, these low-density neutrophils are also found in other disease conditions such as COVID-19, cancer and sepsis, but remain poorly defined.

Long-term impact of Project:

These findings will broaden our understanding of the immunopathogenesis of AAV and will inform future studies that aim to identify potential therapeutic targets in patients with AAV.

Quote:

"I believe that basic scientific research is the foundation of any medical advancement."

Electroencephalographic Biomarkers for Tracking Cognitive Network Dysfunction in Amyotrophic Lateral Sclerosis

PhD Student: Marjorie Metzger

Supervisor: Orla Hardiman (1st supervisor),

Bahman Nasserroleslami (2nd Supervisor)

Funding: Thierry Latran Foundation

Overview of Project:

Treatments research for Amyotrophic Lateral Sclerosis (ALS) focuses mostly on the motor and respiratory aspects of the disease while cognitive and behavioural symptoms impact more than half of the patients (Phukan et al., 2012). Behavioural and cognitive change evaluations are especially challenging in ALS circumstances, as they usually rely on qualitative measurements based on physician's or a family member's report. Quantitative, reliable measures of cognition and social cognition changes would be helpful both for the understanding of the disease's neural mechanisms and the impact of potential treatments. Since previous work showed that high-density EEG measures can quantify neural networks

differences, correlating with MRI findings of structural degeneration and functional clinical scores (Dukic et al., 2019; McMackin et al., 2019; Nasserroleslami et al., 2019), the purpose of this project is to target the neural changes inducing socio-cognitive modifications along the disease progression using quantitative EEG models. Based on resting-state EEG, we explored the two following aims to provide data-driven biomarkers of the cognitive and behavioural consequences of ALS. We studied microstates of resting-state data, as per dynamic analysis and the longitudinal correlation of EEG measures with neuropsychology evaluations to build a multi-modal multi-variable quantitative measure of socio-cognitive impairment.

Long-term impact of Project:

These combined multi-modal quantitative measures of cognitive impairment provide a foundation for clinical quantitative cognitive assessments in ALS, as a measurement tool for future clinical trials

Quote:

"With precise quantitative markers of impairment, we could not only improve understanding of ALS but also find better treatments and hopefully, one day, cure patients."



Does the future of epilepsy care lie in eHealth? An examination of attitudes and behaviours towards epilepsy self-management and eHealth tools from the perspectives of people with epilepsy, their carers, and healthcare providers

PhD Student: Jack Banks

Supervisor: Professor Colin Doherty

Funding: FutureNeuro and S3 Connected Health

Overview of Project:

Using a mixed methods approach – survey, ethnographic fieldwork, semi-structured interviews and focus groups – Jack’s research seeks to understand the barriers and facilitators to digital health adoption for epilepsy self-management. Within the current system of epilepsy care, patients receive their care through periodic face to face appointments in hospital outpatient clinics. With ageing populations and increasing chronic disease prevalence worldwide, there’s a pressing need to innovate care models to alleviate pressure on healthcare systems while maintaining a high quality of care for patients. Both nationally and internationally, it’s recognised that the effective use of technology within healthcare – ‘eHealth’ - is pivotal in shifting care from in-person, acute hospital settings to a more independent, empowered remote model for patients and their carers. This work aims to conceptualise the lived experience of people with epilepsy, their carers and clinicians. Through a behavioural science framework, Jack aims to identify where digital supports can be integrated into the ecosystem of epilepsy care to allow patients to manage their condition more independently.

Long-term impact of Project:

It is important for researchers to gain an understanding of how individuals are using different tools to manage their conditions away from traditional healthcare settings. This will help us in a post-COVID world in designing a healthcare system which combines digital and face-to-face health together in the optimal way.

Quote:

“In the past 12 months, we’ve seen so many disciplines of medicine embrace digital health and remote models of care. Based on my research findings, and from what I’ve read from others in the field, there is little appetite to return to a purely face-to-face model when the pandemic ends.”



Serum resistance of Extra-intestinal Pathogenic *Escherichia coli*

PhD Student: Naoise McGarry

Supervisor: Professor Stephen Smith

Funding: National Children's Research Centre & Trinity College Dublin

Overview of Project:

Bacterial bloodstream infections can result in a chronic and systemic inflammatory response known as sepsis, which poses high morbidity and mortality to those affected. Urinary tract infections caused by extra-intestinal pathogenic *Escherichia coli* (ExPEC) are a predominant cause of sepsis. ExPEC isolates possess virulence factors which confer resistance to the bactericidal components of serum, such as the complement system.

This project aims to identify the complex mechanisms used by a prototypic ExPEC isolate to evade killing by complement. Such mechanisms can include extracellular cell-associated factors, which shield the cell from the immune system, as well as secreted proteins which modulate host immune responses. Naoise's research has identified haemolysin as a virulence factor imparting resistance to serum. Additionally, the complex interplay and regulation of cell-associated virulence factors capsule and O-antigen and their importance in cell integrity as well as serum resistance were characterised. These findings provide further insight into how ExPEC can deceive our immune system and cause systemic infections.

Long-term impact of Project:

Understanding how pathogens cause disease can enable us to find the best approach for prevention and treatment of infection. Identifying the specific virulence factors which are present in sepsis-associated *E. coli* strains provides potential targets for novel therapies and future treatments, such as vaccine development.

Quote:

"If you want to have good ideas, you must have many ideas." – Linus Pauling



What evidence supports the use of art therapy in response to trauma-exposed refugee adolescents, aged 10 to 17 years

PhD Student: Mohannad Ramadan

Supervisor: Associate Professor Dr Ann Nolan and Assistant Professor Kristin Hadfield

Funding: PhD studentship by The Hashemite University in Jordan

Overview of Project:

This research project aims to depict what evidence exists in the literature about marshaling trauma-informed art therapy in refugee adolescents. By providing a comprehensive systematic review of literature, it is expected to in-depth recognize art therapy modalities' strengths, gaps, and challenges in supporting this uniquely vulnerable population against the consequences of trauma exposure. The systematic review will be the foundation stone for a consensus-based Delphi study that will pursue more standardization of art therapy practices in the management of trauma among adolescent refugees through information sharing and obtaining agreements on key statements by a panel of experts in this discipline.

Long-term impact of project:

The refugee population is one of the most devastated groups in all terms, especially on the psychological side, their response to disastrous events, resilience, and adaptation to start a new life. Side by side with the evidence on art and refugees' mental health, I believe practicing and experiencing art and art therapy are revolutionary modalities because of their ability to intelligently reveal trauma manifestations and provide a gentle revenue for

expressing and sharing traumatic experiences and concealed emotions. Throughout our systematic review, we expect to have a clearer image of utilizing and effectiveness of trauma-informed art therapy for refugee adolescents and to stand on the shortcomings. The final product of the Delphi study will be a guideline for the best practice of art therapy to tackle trauma-induced adversities in refugee adolescents. This guideline will help future researchers to produce more robust research, and practitioners and psychotherapists to deliver effective and efficient therapy.

PhD Candidate Quote :

"I spent more than six years working in the provision of medicine and healthcare to refugees and war trauma victims. I always hope to be helpful to them in a broader scope. Now, my hope is renewed by my PhD research. It is another itinerary for contributing to the well-being and health of refugees. I would be proud to see my work cited and implemented by colleague researchers and practitioners to go further with this novel and promising approach."



The mechanisms of sexual dimorphism in allergic disease and chronic spontaneous urticaria

PhD Student: Dr Katie Ridge

Supervisor: Professor Niall Conlon and Professor Cliona O'Farrelly

Funding: Wellcome-Health Research Board ICAT

Overview of Project:

Chronic spontaneous Urticaria and Angioedema is characterised by hives and swelling that last longer than six weeks and can be extremely difficult for patients to manage. It is almost three times as common in females. Katie's research attempts to understand differences between males and females with Chronic Spontaneous Urticaria and Angioedema at a cellular level, which will hopefully inform the understanding of sex differences in disease more broadly. Certain misconceptions exist around this condition. For example, both patients and health care providers can interpret the symptoms as representing evidence of food allergy. This leads to inappropriate testing for food sensitisation and can result in unnecessarily restricted diets and increased patient anxiety. There may be a considerable delay in diagnosis, and patients will typically present multiple times to healthcare providers before a diagnosis is established. In Europe, the mean time to diagnosis is 2-4 years. The condition is treated with antihistamines; however, a high proportion of patients will not respond to antihistamine treatment even at high doses. A specialist, expensive monoclonal antibody drug, Omalizumab, is given on a case-by-case basis and patients require in-hospital administration and support.



Long-term impact of project:

It is hoped that this research will contribute to a growing body of work where sex as a biological variable is placed at the centre of medical research and approaches to treatment.

PhD Candidate Quote :

“My supervisors have been tireless in helping me to achieve this opportunity of an integrated clinical academic training, which as part of the ICAT programme, I am so lucky to have.”

The role of the skeletal muscle pump in the relationship between sarcopenia and orthostatic haemodynamics

PhD Student: Eoin Duggan

Supervisor: Associate Professor Consultant Roman Romero-Ortuno

Funding: Science Foundation Ireland

Overview of Project:

Sarcopenia, an accelerated loss of muscle mass and strength associated with ageing is an emerging global health burden. Orthostatic hypotension, a sustained drop in blood pressure on standing is a common and increasingly prevalent condition in older people and is associated with falls, increased morbidity and adverse outcomes. The relationship between the two disorders is not well characterised despite a possible pathophysiological link via the skeletal muscle pump of the lower limbs which aids venous return during standing via rhythmic muscle activity. This project looks to further investigate that link, firstly in a population cohort of The Irish Longitudinal Study of Ageing looking at the

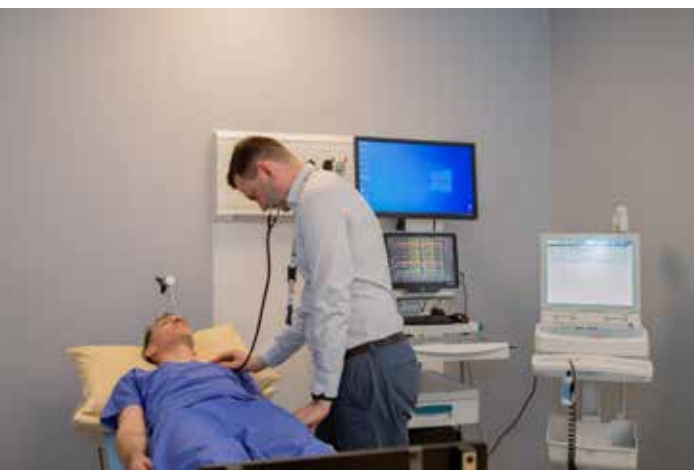
relationship between continuous non-invasive blood pressure measurements taken during standing and markers of muscle strength. Those findings will then be confirmed in a clinical based cohort study from Mercer's Institute of Successful Ageing which will include objective measures of muscle mass and strength and continuous non-invasive blood pressure measurements. Finally, a smaller, healthy cohort of older adults will be recruited to explore the mechanisms underlying the skeletal muscle pump using techniques such as surface electromyography, near-infrared spectroscopy and point of care ultrasound.

Long-term impact of project:

Is it hoped to gain a greater understanding of the mechanisms underlying orthostatic hypotension and the skeletal muscle pump as well as potential modifiable risk factors that can be addressed through physiotherapy, diet and exercise programmes.

PhD Candidate Quote :

"I hope to further our understanding of the skeletal muscle pump and the effects of sarcopenia which is emerging as one of the key healthcare challenges of our ageing population."



An evaluation of the allostatic load framework for quantifying differences in health and longevity

PhD Student: Sinéad McLoughlin

Supervisor: Dr Cathal McCrory

Funding: Health Research Board (HRB)

Overview of Project:

The social patterning of health is well established, with individuals from more disadvantaged backgrounds exhibiting higher rates of disease and earlier mortality than more advantaged peers, yet the underlying age-related mechanisms underlying this association remain unclear. One proposed pathway of investigating this social to biological pathway is the Allostatic Load (AL) framework, which postulates that an accumulation of multi-system physiological dysregulation results from repeated or chronic exposure to stress, leading to a vulnerability to disease and mortality risk. Since its introduction in the early 1990s, research on AL has grown steadily, with multi-system indices of AL shown to be both socially patterned, and predictive of poor health outcomes.

Despite this, no gold standard operational definition exists. This has brought about a large heterogeneity of biomarkers and techniques to instantiate the concept, complicating comparisons of results across studies and stunting the development of the framework. Sinéad's PhD addresses several of the limitations within the extant literature using the rich psychosocial and biological data from The Irish Longitudinal Study on Ageing (TILDA), specifically: (1) whether the method of calculating composite biomarker indices impacts the predictive utility of health outcomes, (2) the extent of the association of life course stress exposure with AL, (3) whether mobility in/out of social disadvantage across the life course moderates AL, and (4) explore the association of a large suite of biomarkers with stress and all-cause mortality to help inform the development of AL indices.

Long-term impact of project:

It is hoped that this research will contribute to a growing body of work on how the social environment comes to impact health.

PhD Candidate Quote :

"I was fortunate enough to be supported and supervised by a passionate researcher, and embedded within an insightful multidisciplinary team at TILDA. I am proud to see my work on Allostatic Load being read and cited by others, and I hope that my research will continue to contribute towards the advancement of the field."



Monocyte development signature in Rheumatoid and Psoriatic Arthritis

PhD Student: Seán Dixon

Supervisor: Dr Viviana Marzaioli

Funding: Science Foundation Ireland (SFI)-Irish Cancer Society (ICS)

Overview of Project:

Inflammatory arthritis (IA), including rheumatoid arthritis (RA) and psoriatic arthritis (PsA), are autoimmune disorders which affect the joints. The pathogenesis of RA and PsA involve a multi-faceted network of cytokines and cellular interactions which influence inflammation and disease progression. Although the two diseases have many common manifestations, their pathogenesis at cellular and molecular level are often different, with studies usually restricted to histopathological methods on the synovium, which often fails to give a detailed understanding on how the diseases work.

Recently, the group have identified differences in the activation, differentiation status and function of monocytes in RA and PsA patients, both in the circulation and at the site of inflammation, which may have an impact in disease progression and therapeutic response. This project will investigate distinct molecular signatures of monocyte development in both RA and PsA, as well as the impact of the joint micro-environment on monocyte signature, employing various high throughput technologies, including RNAseq, 2D/3D cell culture methods, flow cytometry, and epigenetic studies.

Long-term impact of project:

To develop a novel understanding of the innate immune contribution to the differential pathogenesis of RA and PsA, for the identification of new disease markers and drug-candidates for the treatment of RA, PsA and possibly other autoimmune diseases.

PhD Candidate Quote :

“You should never be ashamed to admit you have been wrong. It only proves you are wiser today than yesterday.”



Development of a return-to-work intervention for women with breast cancer

PhD Student: Naomi Algeo

Supervisor: Deirdre Connolly and Kathleen Bennett

Funding: Irish Research Council

Overview of Project:

Naomi's research is focused on cancer survivorship and employment. Specifically, she is developing a programme to support women with breast cancer to return to the workplace after their diagnosis. To do this, the research has been guided by the Medical Research Council Framework for Developing and Evaluating Complex Interventions and involves a number of phases: Phase I: A qualitative-descriptive design exploring what helps and impedes women with breast cancer in transitioning back to work after diagnosis. This involved interviewing women with breast cancer, healthcare professionals and employers across Ireland; Phase II: A systematic review and meta-analysis exploring what rehabilitation interventions are effective in improving work outcomes for women with breast cancer. This involved searching the evidence-base to find out what research has been carried out in the area before, and importantly, what has been found to be effective in supporting work; Phase III: A consensus study to prioritise content and delivery of the programme being developed. This was completed using an online workshop using the nominal group technique and was informed by those living with and beyond cancer, cancer policy informers, cancer support centres, and healthcare professionals; Phase IV: A single-arm feasibility study with qualitative process evaluation. This involves



testing the programme that has been developed and finding out from participants (women with breast cancer) if they found it beneficial or not, if they'd change anything about the programme and if they think it's worth pursuing further in research.

Long-term impact of project:

At present, there are no evidence-based programmes to support return-to-work for those living with and beyond cancer in Ireland. Should the programme be deemed feasible, the next logical step is for further research with larger scale studies.

PhD Candidate Quote :

"I would recommend an academic path to any student. I love the variability and flexibility, the space to read, think, reflect and learn."

Point Of Care Ultrasound For Functional Multi-Organ Evaluation In Neonatal Encephalopathy

PhD Student: Aoife Branagan

Supervisor: Prof Molloy

Funder: Neptune Scholarship Programme - HRB

Overview of Project:

Neonatal encephalopathy results in significant mortality and morbidity in survivors. At present, the only therapy available is therapeutic hypothermia. The hypoxic injury in neonatal encephalopathy is not confined to the brain. The multiorgan injury and systemic inflammation which occurs have been shown to correlate with outcomes.

The use of neonatologist-performed ultrasound is becoming more prevalent in Neonatal Intensive care Units in the diagnosis and management of multiorgan injury. We hypothesise that multiorgan dysfunction evaluation in infants with neonatal encephalopathy will be improved by combining ultrasound, routine

biomarkers and inflammatory indices to predict outcomes and response to therapy. We also aim to assess the use of novel therapeutic agents as adjunctive therapies to therapeutic hypothermia, by assessing their effect ex-vivo effect on the immune function of infants with therapeutic hypothermia.

Long-term impact of project:

Despite the impact of therapeutic hypothermia on outcomes of neonatal encephalopathy, 50% will have disability. We hope that examining the utility of ultrasound in the diagnosis and management of multi-organ dysfunction, with novel biomarkers, will improve multiorgan dysfunction outcomes. We will also assess adjuvant treatment strategies with the hope of improving developmental and health outcomes.

PhD Candidate Quote :

With the help of my supervisor and staff of the maternity hospitals in Dublin, I hope my PhD project will have a positive impact on the care of infants born with Neonatal Encephalopathy



Health Technology Assessment of CD19 CAR T-Cell Therapies in the Irish Healthcare Setting

PhD Student: Niamh Carey

Supervisor: Dr Laura McCullagh and Prof Michael Barry

Overview of Project:

CAR T-cell therapies are innovative treatments for cancer. They are associated with high, upfront costs and a limited evidence base. This creates challenges for key stakeholders, including reimbursement decision-makers. Niamh's research involved conducting independent Health Technology Assessments (HTAs) of the CD19 CAR T-cell therapies, tisagenlecleucel and axicabtagene ciloleucel. Evidence was attained through primary data collections, systematic literature reviews and clinical evidence synthesis, and the use of advanced decision analytic modelling approaches. This evidence informed the bespoke decision analytic models that were developed to evaluate cost effectiveness and budget impacts of these therapies. Value of information analyses were conducted to estimate the value of simultaneously eliminating all uncertainty of all uncertain parameters in the respective cost-utility models. The parameters, which contributed most to the overall decision uncertainty, were identified. The impact of performance-linked reimbursement agreements on the cost effectiveness and budget impact of these therapies was explored.

Long-term impact of project:

The outputs of this research can inform reimbursement decision-making of future CAR T-cell therapies globally. It demonstrates how HTA can inform decisions and can identify areas to be prioritised for future research. It illustrates the value of performance-linked reimbursement agreements in sharing financial risk between the payer and manufacturer. Such agreements have not been widely implemented in the Irish and international settings to date.

PhD Candidate Quote :

“Of all the skills developed over the course of a PhD, I think soft skills such as resilience, adaptability and collaboration are the most valuable.”



The involvement of the immune system in Parkinson's disease

PhD Student: Adina MacMahon Copas
Supervisor: Professor Maeve Caldwell and
Associate Professor Jean Fletcher
Funder: Health Research Board (HRB)

Overview of Project:

Parkinson's disease (PD), is characterized by the progressive loss of dopaminergic neurons in the substantia nigra of the midbrain and accumulation of mis-folded α -synuclein (α -syn) proteins which are also present in the intra-cytoplasmic inclusions, known as Lewy bodies and neurites. Neuro-inflammation is a common feature of PD pathogenesis and recent evidence suggests a potential role for peripheral immune cells in this neuro-inflammatory environment. Reactive astrocytes and microglia are important components of the central nervous system (CNS) immune response; however, dysregulation of these responses is commonly linked to disease pathogenesis, and both have been observed in

PD. Recently, the focus has broadened to include peripheral immune cells, the presence of which has been observed in post-mortem brain tissue of PD patients and has stimulated investigation into their role in the pathogenesis of PD. Once present these cells can contribute to a pro-inflammatory environment and even neuronal cell death highlighting the importance of fully understanding their role in this disease.

Induced pluripotent stem cells (iPSC) represent a useful model for studying this disease as they allow the generation of patient and disease specific neurons and astrocytes, which would be otherwise difficult to obtain. iPSC derived from the dermal fibroblasts of five PD patients will be differentiated into midbrain dopaminergic neurons and astrocytes. Furthermore, peripheral blood mononuclear cells (PBMC) will be isolated from the corresponding PD patient's blood enabling the elucidation of these cellular interactions, and facilitating the investigation of autologous versus allogenic responses between peripheral immune cells, neurons and glia in PD.

Long-term impact of project:

As there are currently no disease modifying therapies for PD, it is only by fully understanding the underlying cellular mechanisms of its pathogenesis that we can uncover novel therapeutic targets for its treatment.

PhD Candidate Quote :

"I hope that this research can provide novel insights into the pathogenesis of Parkinson's Disease and thus eventually guide development of novel therapeutic targets for its treatment."

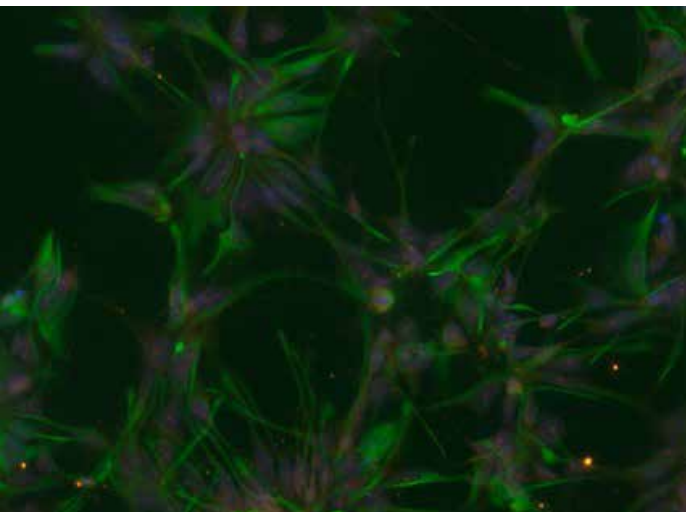


Image: LHS, Human astrocytes differentiated from human iPSC's

Investigating novel therapies for metachromatic leukodystrophy (MLD).

PhD Student: Marianna Mekhaeil
Supervisor: Prof. Kumlesh Dev and
Dr Melissa Conroy

Overview of Project:

Metachromatic leukodystrophy (MLD) is a demyelinating, autosomal recessive genetic leukodystrophy with an estimated birth prevalence of approximately 1–2 per 100,000, and an incidence of 1/40,000 births. MLD is a progressive disease that causes the loss of muscle and cognitive function, as well as progressive loss of vision. Lifespan often depends on the age of diagnosis. In the late infantile form of this disease, death typically occurs within five to six years, while juvenile and adult form may facilitate survival until early adulthood or more. The disease is caused by mutations in the arylsulfatase A gene (ARSA) and consequentially to a deficient activity of the arylsulfatase A lysosomal enzyme. This leads to the accumulation of sulfatides in oligodendrocytes, which result in the dysfunction and destruction of the CNS/PNS (peripheral neuron system) myelin sheaths. Sulfatides also accumulate in visceral organs, pancreas, liver, adrenal glands, lymph nodes and ovaries. Inflammation is a key driver of MLD disease progression, with elevated levels of CCL2, IL-1Ra, IL-8, and macrophage inflammatory protein 1 β (MIP-1 β) in the cerebral spinal fluid of patients with MLD. Various therapeutic approaches to MLD have been tested in experimental animal models but so far, no curative treatment is available. Among the promising approaches with potential clinical utility are: (i) enzyme-replacement therapy (ERT); (ii) bone

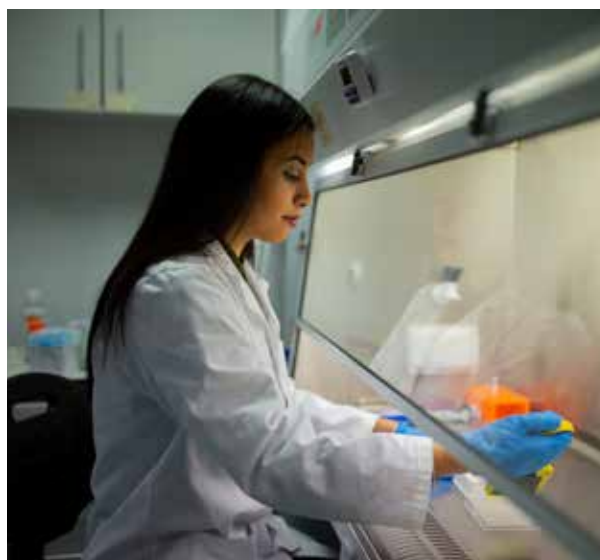
marrow transplant (BMT); (iii) gene therapy by ex vivo transplantation of genetically modified hematopoietic stem cells (HSC); and (iv) AAV-mediated gene therapy directly to the CNS. Marianna's PhD project is investigating the repositioning potential of marketed drugs in 3 different models of MLD; 1) human astrocyte cell line model, 2) murine brain slice model and 3) in vivo mouse model tg/ASA(-/-).

Long-term impact of project:

MLD patients are faced with high mortality rates and a paucity of treatment options are in urgent need of novel drugs. This project uses in vitro, ex vivo and in vivo model to test the utility of FDA-approved therapies for MLD and ultimately improve outcomes for this patient cohort.

Quote:

"I believe that drug repositioning may provide new treatment opportunities for debilitating diseases, for which there are a paucity of treatment options and an urgent need for novel therapeutic approaches."



Physical activity, physical health and clinical phenotype in adults with moderate and severe haemophilia.

PhD Student: Megan Kennedy

Supervisor: Professor John Gormley

Funder: Science Foundation Ireland and Takeda

Overview of Project:

Haemophilia is an inherited bleeding disorder caused by a deficiency in procoagulant Factor VIII (Haemophilia A) or Factor IX (Haemophilia B). People with moderate and severe haemophilia (PwMSH) may experience spontaneous or trauma-induced bleeding into joints and muscles, which cause significant pain and physical disability. Furthermore, repetitive joint bleeding in the long-term causes synovitis and osteochondral destruction resulting in a degenerative joint disease known as 'haemophilic arthropathy,' which causes further chronic pain and physical disability. PwMSH were previously discouraged from participating in physical activity (PA) due to the perceived risk of bleeding and joint injury. Regular PA is associated with numerous health benefits, including improved physical fitness and reduced chronic health risk. Improvements in haemophilia treatment over recent decades have enabled PwMSH to become more physically active, and tailored PA is now strongly recommended for PwMSH. Adult PwMSH, however, may still face challenges in achieving regular PA due to chronic pain and physical disability caused by historical bleeds and established arthropathy. This may impact their overall physical fitness and chronic health risk with ageing. The aim of this PhD was to undertake a detailed examination of PA, physical health and the clinical phenotype of adult PwMSH in Ireland.



Long-term impact of project:

The overall findings of this PhD identified lower levels of PA and physical fitness in PwMSH compared to controls, in addition to other significant cardiometabolic risk factors, and various barriers to PA. These findings will be useful for informing the design of personalised, multi-disciplinary health interventions, which aim to improve chronic health risk and quality of life amongst the ageing haemophilia population.

PhD Candidate Quote :

"I will be forever grateful for the generosity and enthusiasm of all of the participants who supported this research. I hope that the valuable insights they have provided us with will positively impact physical activity and physical health amongst the ageing haemophilia population."

Symptomatic hypermobility in children: a move towards improved care pathways and targeted treatment

PhD Student: Susan Ward

Supervisor: Dr Sara Dockrell and

Dr Emma McDermott

Funder: National Children's Research Centre

Overview of Project:

Susan is researching children with joint hypermobility-related disorders. Joint hypermobility is the term used to describe the capability that a joint has to move beyond normal limits. For most children, hypermobility causes no problem. However, some children complain of pain in multiple joints and muscles, frequently worse towards the end of the day following activity. They may complain of fatigue or difficulties with functional tasks which can limit their ability to participate in daily activities (such as attending school or doing sport and physical activity). Symptoms often extend beyond the musculoskeletal system into the gastrointestinal, cardiovascular,

urogenital, and psychological domains. This varied pattern of symptoms can present a challenge and delays in terms of diagnosis and treatment. Exploring this range of symptoms in children is an important part of Susan's mixed methods research to help us understand the condition and the full impact of it on the children's quality of life. Susan intends to assess the clinical characteristics in participants diagnosed with symptomatic hypermobility using a cross-sectional quantitative study. Additionally, semi-structured interviews will be used to explore the impact of symptomatic hypermobility on children and their families. She hopes to develop a decision-making tool for use in the clinical setting.

Long-term impact of project:

The team hope to inform and influence future care pathways for children with symptomatic hypermobility who currently experience long delays in diagnosis and management.

Quote:

"Following my PhD, as a research active health professional, I hope to encourage others to engage in meaningful research in their own clinical areas of expertise."



Coercion and Involuntary Care: A Study of Involuntary and Voluntary Psychiatry Inpatients in Dublin

PhD Student: Aoife O’Callaghan

Supervisor: Professor Brendan Kelly

Overview of Project:

This research aims to examine how patients feel they have been treated in hospital. Specifically, it looks at coercion among voluntary and involuntary psychiatric inpatients. Coercion means being forced to do something. The study looks at whether or not people receive psychiatric care in a way that makes them feel respected. It will attempt to assess perceived levels of control, choice, respect, privacy, attitudes towards medication and satisfaction with treatment. The results obtained aim to provide a clear picture of patient’s own experiences during treatment, providing important information that will help to shape future revisions of clinical policies and procedures.

This study will examine coercion and perceived procedural justice in relation to involuntary and voluntary psychiatric admission. The first objective is to determine levels of perceived coercion among involuntary and voluntary psychiatry inpatients in Tallaght Acute Psychiatry Unit and Connolly Acute Psychiatry Unit, and relate these to variables such as age, gender and diagnosis, attitudes to treatment and therapeutic alliances.

Long-term impact of project:

Inpatient admission is a common feature of mental health services worldwide. This research aims to provide a greater understanding of the demographic and clinical correlates of admission status and associated perceived coercion in order to provide evidence to inform policy in this setting.

PhD Candidate Quote :

“Being supported to pursue this research and have exposure to the academic side of psychiatry while continuing to work clinically has been an invaluable experience.”



Development and testing of the acceptability and feasibility of a multicomponent intervention to reduce sedentary behaviour in a workplace setting

PhD Student: Gail Nicolson

Supervisor: Associate Professor Catherine Darker and Professor Catherine Hayes

Funding: Dean of the Faculty of Health Sciences, Trinity College Dublin

Overview of Project:

Over the course of our day, we spend more than seven hours being sedentary, and for most adults, sedentary behaviour mainly occurs in the office workplace. This behaviour puts our health at risk, and the evidence shows that sedentary behaviour is associated with the development of cardiovascular disease and cancers and may lead to a higher risk of death. In particular, workplace sitting appears to be associated with a higher risk of developing pancreatic, lung and breast cancers. Workplace interventions may be important strategies in our efforts to reduce sedentary behaviour and increase physical activity in those who are most at risk. Multiple short bouts of physical activity (rather than long exercise sessions) are likely to be practical and acceptable in the workplace, and evidence suggests that these short sharp bouts of exercise may actually benefit us more. The aim of Gail's study was to assess the acceptability and feasibility of a gender-sensitive intervention, guided by the socio-ecological model, to reduce sedentary behaviour among professional men in two workplaces. The main influences of sedentary behaviour were targeted: at the individual level (behaviour change techniques such as goal-setting, self-monitoring), social (collegial support and competition), environmental (change to the workstation), and organisational (management

support). Men were each provided with a Garmin watch and the associated web-based/smartphone application, Garmin Connect. An under-desk pedal machine was also provided for the duration of the intervention. Managers were recruited to provide support to the employees.

Long-term impact of project:

The Cycle at Work intervention has the potential to change workers' behaviour by increasing light physical activity. The findings of this research may have significant impact on national policy.

Quote:

"Given that the typical workplace is highly sedentary in nature, and that employees and organisations have the authority to implement their own policies, the 'Cycle at Work' intervention has the potential to effect real change. This multicomponent intervention could be offered to both employers and employees as part of a wider culture of wellness."



Delivering equitable healthcare access for adults experiencing homelessness

PhD Student: Rikke Siersbaek

Supervisor: Professor Steve Thomas; Dr Sara Burke; Dr Cliona Ní Cheallaigh

Funding: Structured Population and Health-Services Education Programme (SPHERE), funded by the Health Research Board

Overview of Project:

Rikke's research aims to understanding how health services are funded, organised, accessed, and delivered from a population health perspective. Within that broader area, she is interested in health inequalities and how health systems facilitate or impede healthcare delivery for vulnerable populations. In particular, Rikke's PhD research asks how, why, for whom and to what extent health systems factors, such as funding, planning, performance management, service design and culture, impact on healthcare access for populations with complex needs experiencing homelessness.

Long-term impact of project:

The overall goal is to influence policy makers who plan and design health services by demonstrating the upstream factors that impact healthcare accessibility for vulnerable populations. Health services can be funded, organised and delivered in ways that make access easier, and healthcare practitioners can be trained to work in ways that promote accessibility and create the right culture in which services can be equitably accessed.



PhD Candidate Quote :

“I enjoy research and think it is a wonderful, engaging, and challenging career choice. But it is a means to an end – providing evidence to policy makers, practitioners, and managers is crucial.”

GxE interactions in skin cancer and vitamin D status

PhD Student: Rasha Shraim

Supervisor: Professor Lina Zgaga and

Professor Ross McManus

Funding: Science Foundation Ireland Centre for Research Training in Genomics Data Science; Marie Skłodowska-Curie Actions COFUND

Overview of Project:

Broadly, Rasha is interested in understanding the interplay of genetics and environment in determining health outcomes. Her research focuses on the effect of sun exposure and genetics on two opposing outcomes: vitamin D status, which benefits from sun exposure and skin cancer risk, which may be worsened by sun exposure. Rasha applies computational and statistical methods to genetic, health, and environmental data from a large UK cohort of approximately half a million people. The goal is to identify genetic or environmental patterns that affect vitamin D status or skin cancer risk and that can eventually be used to inform public health advice around sun protection, supplements, or cancer screenings.

Long-term impact of Project:

Evidence-based public health advice on sun exposure for vitamin D status and for skin cancer tailored to the affected population and its environment.

Quote:

“I hope that this project will contribute to our understanding of the role of vitamin D in human health and, more broadly, promote a more integrative approach to studying genetics and environmental exposures in health research.”



Interactive monitoring of paediatric outcome reporting for radiation and chemo therapies (IMPORT)

PhD Student: Mr. Graham Kelly

Supervisor: Dr Michelle Leech and Dr Laure Marignol

Funder: Irish Research Council

Overview of Project:

The hypothesis of Graham's project is that merging the motivational benefit of gamification with the clinical benefit of patient reported outcome measures (PROMS) can improve side effects reporting in paediatric cancer patients aged 8-12 undergoing treatment. IMPORT will transform a PROMS questionnaire for oncology into a child-friendly game and carer educational platform shared with clinicians. IMPORT aims to prove the concept that introducing gamified PROMS during clinical management of children addresses their side-effect communication needs, supports their families, and assists clinicians.

The side effect communication needs of paediatric oncology patients and their families are currently insufficiently met. Traditionally, parents act as proxies for children and relay symptom information, imparting their interpretation of how their child is feeling. Depending on age, the child may also be questioned. Gamification adds video game elements to non-gaming contexts and has been introduced to assist patients, their families, and clinicians in monitoring treatment side effects in paediatric oncology in a limited fashion. This is in line with the play-based principles routinely used in paediatric medicine. Persistent reports of limited reporting

of paediatric patients' treatment side effects demonstrate that further innovation is required and this is what IMPORT will deliver.

Long-term impact of Project:

IMPORT will bring about a paradigm change in how paediatric patients report their symptoms and will enable children to have their voice heard during their cancer treatment. IMPORT will make future cancer treatment side effect reporting child focused, yet family-centric.

Quote:

"IMPORT will develop a novel video-gamified patient reported outcome system for children aged 8-12 to allow their voice to be better represented throughout their care."



Targeting metabolism for individualised rectal cancer treatment

PhD Student: Croí Buckley

Supervisor: Dr Niamh Lynam-Lennon and
Professor Jacintha O’Sullivan

Funding: Health Research Board

Overview of Project:

Croí’s research focuses on the role of cellular metabolism in the response of rectal cancer to radiation therapy. Colorectal cancer, or bowel cancer, is the 3rd most common cancer type in Ireland, with a third of bowel cancers occurring in the lower bowel (rectum). A combination treatment of chemotherapy and radiation therapy is an effective treatment strategy to reduce tumour size before surgery for some rectal cancer patients. Unfortunately, for a large number of patients this strategy is ineffective, and can have detrimental effects, including delays to surgery and therapy-associated toxicity. Recently the research team demonstrated that cancer cell metabolism (how cancer cells make their energy to survive and grow) is associated with poor response to radiation therapy in oesophageal cancer. Croí’s project follows on from this research, by investigating altered energy metabolism in rectal cancer and the link between these metabolic changes and radiation resistance. The research team are also investigating whether they can boost poor responses to radiation therapy by repurposing drugs which affect energy metabolism, such as Metformin (a drug commonly used to treat type II Diabetes) as a radiosensitiser in cancer.

Long-term impact of Project:

Thanks to pre-treatment blood and tissue biopsies, generously donated by patients with and without cancer, this research contributes to the growing scientific knowledge of rectal cancer and therapeutic resistance. The multi-omic profiling being conducted on patient samples will lay the groundwork for future pre-clinical and clinical studies in the field of gastrointestinal cancers and therapeutic resistance.

Quote:

“A career in research provides a wonderful outlet to combine innate curiosity and problem solving while also contributing to a very worthy cause.”



Enhancing immunotherapy in Oesophageal Adenocarcinoma through the modulation of immunometabolism with novel small analogue inhibitors

Quininib and its analogues

PhD Student: Andrew Sheppard

Supervisor: Professor Joanne Lysaght

Funding: Irish Research Council and Cross Charity

Overview of Project:

Andrew's research focuses on using a new type of therapy for oesophageal cancer. This new therapy is called immunotherapy and uses your body's own natural defence system to fight cancer. The problem is that, just like chemotherapy or radiotherapy, it does not work for some people. Andrew's project aims to understand why this happens and at the same time, attempting develop a new drug that they hope can help improve how patients respond to treatment. The science of it relates to how our cells need to consume nutrients for energy, just like ourselves. The problem is that cancer cells consume food at a higher rate leaving other cells, such as the cells of our immune system, without enough nutrition to carry out their role properly. The research team's aim is to target the metabolism of cancer and immune cells in the hopes of boosting the ability of the immune cells to kill the tumour cells alongside conventional therapy and the new immunotherapies.

Long-term impact of Project:

By closely partnering with patients, other research groups, and clinicians, the team hope to lay the foundations for future pre-clinical and clinical studies.



Quote:

“Studying towards a PhD is an exciting path where you have a certain freedom to follow wherever your experimental findings lead, something a lot of other careers could not offer.”

Directory of active MD and Doctoral Research Projects 2022-2028

Anatomy

- PhD Investigating the impact of ketone body supplementation on the growth and development of cortical neural stem cells and neuroblastoma

Clinical Medicine - Nanomedicine

- PhD 3D model for safety assessment of nanobiomaterials
- PhD Hyperthermia treatment applied to cancer
- PhD In-vitro models of NSCLC that effectively mimic angiogenesis processes in humans

Clinical Medicine - TB immunology

- PhD Identifying Macrophage Immune Defects In Susceptible Hosts – A Mycobacterium tuberculosis and HIV Co-infection Model
- PhD “Exploiting Immunometabolism in Tuberculosis (EXTINCT)”

Clinical Medicine

- PhD Supporting physical function in community-dwelling older adults – a focus on health inequalities and underserved groups
- PhD Defining immune phenotypes in septic patients to Immunological endotyping of critical illness to understand the sepsis-induced immune-paralysis state after severe sepsis in patients with cancer-related versus non-cancer-related sepsis
- PhD Microcirculation in fluid resuscitation in sepsis
- PhD Investigating the role of SARM1 in retinal degeneration
- PhD Investigating the impact of immune senescence in Age-related Macular Degeneration
- PhD Characterisation of TLR2 function in subretinal macular fibrosis
- PhD Defining the consequence of innate immune training on protective versus pathogenic T cell responses in patients with Tuberculosis
- PhD The Fight for Iron at Mitochondria: Implications for Respiratory Infection and Disease
- PhD Iron and its Ferocious role in alveolar type II epithelial cell dysfunction in chronic lung diseases
- PhD Defining the role of Th17 lineage cells in human pulmonary health and disease
- MD The pathogenesis of Hidradenitis Suppurativa
- MD Assessment of xerostomia management strategies in patients with advanced cancer
- MD Outcomes of Paediatric Inclusion Health
- MD Oral Symptom Assessment Scale (OSAS): Validity and Reliability

- MD To identify predictive biomarkers of non-infectious pulmonary complications post bone marrow transplantation
- MD The effects of Reslizumab Therapy in Severe Eosinophilic Asthma
- MD A study of Doppler Ultrasound in the diagnosis and monitoring of Giant Cell Arteritis (GCA)
- MD The effects of corticosteroids on human macrophages infected with Mycobacterium tuberculosis
- MD A study on cardiac pacing and cognition
- MD HDL cholesterol efflux capacity (HDL-CEC), HDL lipoprotein function and lipidomic analysis in T1DM and risk of atherosclerosis
- MD Prevalence of and Interventions for Fatigue in Patients with Inflammatory Bowel Disease
- MD Hyperuricaemia as a marker of future metabolic and cardiovascular disease
- MD Assessment and Management of Pancreatic Cysts
- MD An Evaluation of Epilepsy and Driving in Ireland including Patient Impact, Understanding among Healthcare Professionals, and Digital Resource Development

Clinical Microbiology

- PhD The extracellular glycome of Extraintestinal E. coli
- PhD Bacteriophage therapy of E. coli
- PhD Genomic landscape of neonatal E coli sepsis
- PhD An Investigation into the Role of Pigs in the Epidemiology of Human Clostridioides difficile Infection
- PhD Antisocial Behaviour in the Cystic Fibrosis Airway Microbiome
- PhD The impact of antifungal treatments on the killing activity of immune cells against Aspergillus fumigatus
- MD A study of Mycobacterium bovis infection

Clinical Nephrology

- PhD Investigation of Molluscum Contagiosum Virus inhibitor of both NFkB and IRF signalling MC009.
- PhD Investigation of Molluscum Contagiosum Virus inhibitor MC089 which targets IRF activation
- PhD Investigation of Molluscum Contagiosum Virus inhibitor MC008 which targets human DNA sensing.
- PhD Metabolomic analysis of monocytes in ANCA Vasculitis

PhD	Phenotype and Function of Neutrophil subtypes in ANCA vasculitis
PhD	Cross- Disease Assessment of Phenotypic and Functional Granulocyte Heterogeneity
PhD	VAPRE: Exploring the Relapse Prodrome of ANCA associated Vasculitis

Gastroenterology

MD	A study of clinical scores, investigation and management of gastrointestinal bleeding
MD	An investigation of completion rates in capsule endoscopy

Haematology

MD	Determinants of Immune Reconstitution After Allogeneic Haematopoietic Stem Cell Transplantation Performed With Anti-T-Lymphocyte Globulin
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Health Policy & Management

PhD	Osteoporosis in Irish men: Cost-of-illness, a qualitative exploration and preliminary economic evaluation of reducing the burden of illness.
PhD	Costs of screening and diagnostic services and resource requirement for colorectal cancer screening in Ireland
PhD	Enhancing the Evidence Base for Cost-Effectiveness Analysis in Ireland: Building Improvements from the Intervention-Specific to System-Wide Level
PhD	Assessing the cost-effectiveness of Psychosocial Interventions for Advanced Cancer Patients and their Informal Caregivers
PhD	Facilitating readiness for advance care planning in Ireland: Informing the design of a health behaviour change e-intervention for older people in the community.
PhD	Exploring policy amenable factors across the medical device lifecycle impacting patient safety: a multi-method study'
PhD	RESTORE PhD Scholar Arianna's PhD is on staff engagement.
PhD	Delivering equitable healthcare access for adults experiencing homelessness
PhD	The relationship between staffing and the occurrence of hospital acquired infections in Irish public acute hospitals

Histopathology

PhD	Biomarkers for cervical cancer
PhD	Investigating Enzalutamide resistance in prostate cancer
PhD	Enhanced AI enabled digital pathology
PhD	HRD in ovarian cancer

MD	A prospective case control study of concurrent Non-alcoholic fatty liver disease (NAFLD) and Inflammatory bowel disease (IBD)
MD	A multilayer investigation of the interaction between HPV, TLRs (4, 7, 9), MyD88 and endosomal trafficking in a panel of HPV positive and HPV negative cervical carcinoma cell lines and cervical tissue specimens
MD	A pilot study to identify novel biomarkers of response, resistance and toxicity of Immune checkpoint inhibitors (ICI)

Immunology

PhD	Development of a bioanalytical platform to monitor immune reconstitution post allogeneic stem cell transplantation and post CAR-T therapy
PhD	The role of mast cells in chronic urticaria
MD	Non immunological risk factors associated with prior Staphylococcus aureus infection

Medical Gerontology

PhD	Socioeconomic position, physiological dysregulation and poor health outcomes; a life course perspective using data from Ireland
PhD	Clinical Decision Support Combining Cerebral Perfusion and Machine learning in Falls and Syncope Management
MD	Analysis of clinical outcomes from a video-enabled nursing home education programme, and the subsequent derivation of topics for a nursing home staff education curriculum through assessment of ED attendance patterns and Delphi consensus discussion.
PhD	Investigating the role of the innate immune system in ageing-associated pathophysiology: implications for anti-viral immunity and COVID-19
PhD	The age old problem of ANCA vasculitis
PhD	Using Systems Immunology to Characterise Variability in Anti-Viral and Vaccine-Induced Immune Responses in Older Nursing Home Residents: Towards Next-Generation Vaccine Design and Deployment Strategies
PhD	Investigation of the role of the muscle pump in orthostatic hemodynamics
PhD	Nutrition and Ageing
PhD	Characterising appropriate cardiometabolic clinical care for older community-dwelling people"
PhD	Clinical Utility of Cerebral Perfusion in Syncope and Falls
PhD	Cerebral hemodynamics in older adults: relationship with ageing, disease and health behaviours
PhD	Metabolic syndrome, chronic low-grade inflammation, accelerated ageing, cognitive impairment and frailty".
PhD	Investigation of physiological reserve via assessment of performance in physical tasks using explainable machine learning

PhD	Modifiable risk factors for dementia and their impact on cognition and gait in patients with mild cognitive impairment attending a memory clinic”
PhD	Polypharmacy and potential inappropriate prescribing in community dwelling people living with dementia.
MD	The neuroscience of frailty
MD	Teaching of stroke medicine to undergraduate medical students
MD	Investigation of Bone Health in TUDA and TILDA
MD	Analysis of clinical outcomes from a video-enabled nursing home education programme, and the subsequent derivation of a comprehensive nursing home staff education curriculum through assessment of ED attendance patterns and delphi consensus discussion
MD	An investigation of the capability of the Reveal LINQ™ Falls Prediction Research System to identify early changes in physiological parameters as risk predictors of falls
MD	Influence of frailty on hypertension management outcomes in TILDA
MD	Nursing home residents attending the acute hospital before and during a pandemic: clinical characteristics and outcomes, and impact of a specialist intervention team to manage care
MD	Cardiovascular Autonomic Function and Response to Aortic Valve Replacement
MD	The longitudinal impact of microstructural integrity of white matter hyperintensities

Molecular Rheumatology

PhD	Stromal cell subtypes define distinct pathogenesis in RA and PsA
PhD	Differential pathogenic mechanisms drives stromal cell interactions and invasive pathways in RA & PsA.
PhD	Targeting metabolic pathways induces resolution of inflammation in Rheumatoid Arthritis
PhD	Macrophage signatures that distinguish RA and PsA pathotypes - impact for disease progression and response.
PhD	Monocyte development signature in Rheumatoid and Psoriatic Arthritis
PhD	Arthritis in Children with Down’s Syndrome is a Distinct and a more Pathogenic Disease Compared to Juvenile Idiopathic Arthritis

Neurology

PhD	Multimodal analysis for brain network fingerprints in Parkinson disease patients
PhD	Novel Non-invasive Assessment of the Spinal Cord Electrical Activity for Neurological Diagnosis

PhD	Pin-Pointing the Weakest Link in Network Collapse in Amyotrophic Lateral Sclerosis: Multi-Modal Neurophysiological Biomarkers of Disrupted Cortical Connections for Patient Selection and Intervention
PhD	Finding neurophysiological Biomarkers of cognitive network dysfunction across neurodegenerative diseases: differential diagnostics, novel re-phenotyping, and clinical trial design
PhD	Identifying Neurophysiological Biomarkers of Altered Sensorimotor Integration in ALS: A multi-modal approach based on EEG, TMS, and peripheral stimulation
PhD	Digitising Measurement of Function in Amyotrophic Lateral Sclerosis
PhD	Advancing the translation of circulating biomarkers for the management of chronic and rare neurological diseases
PhD	Tuberous Sclerosis Complex (TSC) The Experience in Ireland
PhD	An Exploration of the Neurological Manifestations of Non-Cirrhotic Chronic Hepatitis C Infection in Ireland in the Direct-Acting Antiviral Era
PhD	Does the future of epilepsy care lie in eHealth? An examination of attitudes and behaviours towards epilepsy self-management and eHealth tools from the perspectives of people with epilepsy, their carers and healthcare providers
PhD	Network Impairment in ALS: Quantifying the Unquantifiable
PhD	Characterising the cognitive profile of presymptomatic neurodegenerative movement disorders and their endophenotypes
PhD	Resting State Biomarkers of Network Dysfunction and Patient Phenotyping in Amyotrophic Lateral Sclerosis
PhD	Assessing Lower Motor Neuron and Cortical Networks in Motor Neuron Disease using Cortico-Muscular Coherence and MUNIX
PhD	Clinical Heterogeneity in Monogenic Neurodegenerative Diseases: an exploration of potential endophenotypes and genetic modifiers in patients and their relatives
PhD	Neuroimaging Features of Amyotrophic Lateral Sclerosis
PhD	Cerebral changes in poliomyelitis survivors: a computational neuroimaging study

Obstetrics

MD	Lymph Node Status and Coagulation Biomarkers as Predictors of Venous Thromboembolism In Gynaecological Cancer Patients Post Surgery
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Occupational Therapy

PhD	Using Rasch analysis to refine the psychometric properties of the Electronic Trinity Student Profile (eTSP; Nolan, 2011)
PhD	The Experience of Autistic women in Navigating the World of work
PhD	Testing the Effectiveness of “Fatigue and Activity Management in Work” (FAME-W) Intervention for Individuals with Inflammatory Arthritis
PhD	Use of link workers to provide social prescribing and health and social care coordination for people with complex multimorbidity in socially deprived areas.
PhD	Development of a return to work intervention for women with breast cancer
PhD	The process of discharging stroke survivors from physiotherapy stroke care: The physiotherapist perspective
PhD	Support exchange between patients and family caregivers in palliative care
PhD	An exploration of the mealtime experience for family carers of people with motor neurone disease
PhD	The Development of a complex occupational therapy intervention for neonatal units in Ireland
PhD	An exploration of Occupational Therapy Practice with Children experiencing Complex Trauma

Oncology

MD	An evaluation of the immune-metabolic signature of visceral obesity on tumour microenvironment in the setting of colorectal carcinoma
MD	Evaluation of Clinical, Genomic and Tissue Microenvironment Secretion Profiles Associated with Ustekinumab Response in Inflammatory Bowel Disease Patients

Ophthalmology

MD	Automated deep learning in retinal images
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Paediatrics

PhD	PUFFIN: Point of care ultrasound for functional multi-organ evaluation in neonatal encephalopathy.
PhD	CRADLE: Circadian Rhythm Alterations and outcomes in neonatal Encephalopathy
PhD	PANDA: Psychological And NeuroDevelopmental Assessment of Neonatal Encephalopathy
PhD	FIREFLY project: follow up of inflammatory responses and multiorgan outcomes FoLLowing neonatal brain injurY
PhD	PLATYPUS: Preterm Inflammatory Hyperreactivity and response to pentoxifylline to understand necrotising enterocolitis and sepsis.

PhD	DREAM project: Down syndRome, nEurodevelopment And Multiorgan outcomes: TCD
PhD	NIMBUS project co-ordinator and GENIE: Gender differences in preterm neonatal outcomes and mechanisms of altered immune function
PhD	T Cell Phenotype in Neonatal Brain Injury and Followup in Childhood.
MD	A Single-centre, Prospective Study in Paediatrics Fontan Patients evaluating impact of regular aerobic and strength exercise regime on exercise capacity and ventricular function and perceived quality of life

Psychiatry

PhD	Mental Capacity for Treatment Decisions in Psychiatric Inpatients
PhD	Dignity, Coercion and Involuntary Care: A Study of Involuntary and Voluntary Psychiatry Inpatients in Dublin
PhD	The Indian Mental Healthcare Act 2017. Evaluation of the act, its context and its initial implementation
PhD	Admissions to St Patrick’s Hospital 1900 to 1950: from bromides to convulsive therapies
PhD	Identification of Rare Variants from Whole Genome Sequence Data in Family Studies of Psychiatric Disorders
PhD	Longitudinal neuroimaging in children with ADHD
PhD	Predicting who will respond to stimulant medication in ADHD: A precision medicine approach using neurally informed computational models
PhD	Towards an understanding of the mechanism of action of methylphenidate in ADHD
PhD	Predicting who will respond to stimulant medication in ADHD: A precision medicine approach using neurally informed computational models
PhD	The Contribution of Other hits to ND-CNV Carrier Neurodevelopmental and Neuropsychiatric Phenotypes
PhD	Inflammatory markers of antipsychotic weight gain and cardiometabolic dysfunction in youth mental health disorders
PhD	Influences of social cognition and reward processing on autism symptoms in Prader-Willi Syndrome
PhD	Ancient and modern population genomics on the peopling of East Eurasia and the Americas
PhD	Genomic landscape of neonatal Escherichia coli associated sepsis in Ireland
PhD	Shame and Child Sexual Abuse
MD	Updated longitudinal approach to the Penrose hypothesis: a 25-year dynamic ecological analysis of psychiatric hospital admissions and prison committals
MD	Outcomes of inpatients detained under holding powers in an Irish Psychiatric Hospital – A Comparative Case-Control Study

MD	Asclepiades' medical theory of "molecules" and "void spaces" as it relates to Mental Illness
MD	An investigation of the prevalence rates of mental illness in older adults admitted to hospital in Ireland and assessment of current Old Age Liaison Psychiatry service provision
MD	Impact of the Covid-19 pandemic on nursing home staff in Ireland
MD	To characterise the effects of Anorexia Nervosa (AN) on biological ageing

Pharmacology & Therapeutics

PhD	The Impact of Health Technology Management in the Irish Healthcare Setting.
PhD	Health Technology Assessment of CD19 CAR T-Cell Therapies in the Irish Healthcare Setting
PhD	Investigating the effects of a natural multi- mineral extract from red marine algae in innate immune cells
PhD	Role of PP2A in modulation brain microvascular endothelial cell function

Physiology

PhD	The brain-muscle loop: using exercise to target neuroinflammation
PhD	Sports Concussion and Brain Health: The need for Objective and Diagnostic Tools of Pathological Brain Indices.
PhD	Analyzing the role of microglia on the neurological outcomes after birth asphyxia
PhD	Targeting endosomal TLR signalling and inflammasome activation with cannabinoids in immune cells with relevance to Multiple Sclerosis
PhD	Developing inflammasome assays in MS
PhD	Terpene/cannabinoid modulation of endosomal TLR signalling in immune cells
PhD	The effects of antipsychotics on glial cells, neuroinflammation and demyelination.
PhD	Investigating sex differences in the role of T cells in AD
PhD	Assessing the contribution of the AMPA receptor to physiological and pathophysiological brain rhythms in vitro'.
PhD	Effects of early-life experiences on microcircuitry in avian forebrain areas involved in stress regulation'
PhD	"Decoding neuroinflammatory effects on neuronal circuits at the interface of dementia and delirium
PhD	Investigating novel therapies for metachromatic leukodystrophy (MLD)
PhD	Contributors of discrete dopaminergic neurons to the modulation of memory strength

Physiotherapy

PhD	Feasibility and evaluation of a school-based physical activity intervention targeting low-income, urban adolescent females in Ireland
PhD	The Role of Intermediaries in Connecting Primary Care Patients to Community Physical Activity and Sport
PhD	Work-based assessment: Translating theory to practice in allied health professionals
PhD	Exploring physical activity in Maltese Children
PhD	Bike fit for performance and safety in elite cycling
PhD	Back pain in adolescent sport
PhD	Safety and optimal tackle outcomes in women's rugby
PhD	Heart rate recovery responses and Active Stand Protocols
PhD	An Investigation of Physical Activity, Physical Health and Clinical Bleeding Phenotype in Adults with Moderate and Severe Haemophilia in Ireland.
PhD	The effects of nutritional intervention combined with exercise in the ReStOre II (Rehabilitation Strategies following Oesophago-gastric Cancer) program.
PhD	The Role of Exercise Prehabilitation Prior to Oncological Resection
PhD	Childhood symptomatic hypermobility: a move towards improved care pathways and targeted treatment
PhD	A National Adolescent Idiopathic Scoliosis Physical Wellbeing Study.

Public Health & Primary Care

PhD	How Local Decision Making Works for Adaptations of Health Interventions During Scale-up: A Realist Review
PhD	Evaluation of feasibility and health impacts of social prescribing in a general practice setting
PhD	Development and testing of the acceptability and feasibility of a multicomponent intervention to reduce sedentary behaviour in a workplace setting
PhD	Measurement of 25-hydroxyvitamin D in hair
PhD	The role of gene-UVB interaction on 25-hydroxyvitamin D level and skin cancer
MD	Mental Health Services and Homeless people in the Dublin Region; a cross sectional study
MD	Exploring the physical, psychological and social effects of chemsex, enabling the development of a specialised service, and the integration of affiliated services in Ireland

Radiation Therapy

PhD	Tumours have a sex: impact on the response of bladder cancer to therapy
PhD	Modelling of toxicity in non-small cell lung cancer
PhD	Barriers to access in radiation oncology (BARO project)
PhD	Using radiomics to predict normal tissue toxicity in head and neck cancer
PhD	KAYAc- Knowledge of late effects of cancer therapy for adolescents and young adults
PhD	IMPORT- Interactive monitoring of paediatric outcomes for radio and chemo therapies

Surgery

PhD	Effect of radiation in visceral adipose tissue in Oesophageal Cancer patients
PhD	Boosting oxygen diffusion in the radioresistant Oesophageal tumour microenvironment to improve radiation response.
PhD	Immunophenotyping of pancreatic cystic lesions
PhD	Enhancing anti-tumour immunity in Oesophageal cancer through the modulation of immunometabolism with the novel small molecule inhibitor Quininib and its analogues
PhD	in patients with upper gastrointestinal cancers.
PhD	Harnessing the power of the immune system to fight obesity-associated cancer
PhD	Therapeutically remodelling the immune profile of 'cold' tumours in obesity-associated cancer.
PhD	Investigation of the role of miRNA in the treatment resistance of gastro-oesophageal cancer
PhD	Targeting metabolism for individualised rectal cancer treatment
PhD	Investigation of the role of the complement system in treatment resistance of rectal cancer
PhD	Role of miR-31 in modulating chemoradiosensitivity in pancreatic adenocarcinoma
PhD	Multi-omics in stratifying risk in patients with pancreatic intraductal papillary mucinous neoplasms
PhD	Developing and Feasibility Testing of a Pragmatic, Patient-Centred Exercise Intervention During Chemotherapy: A Mixed-Methods Approach
MD	To create, co-design and evaluate a digital learning platform, Burkittpedia
MD	Cellular and peptide components of both CSF and venous blood pre and post dorsal root ganglion pulsed radiofrequency treatment: single-centre, randomized controlled trial

Doctoral Funding Sponsor Acknowledgements

Doctoral Funding Sponsor Acknowledgements

Breakthrough Cancer Research

Cross Charity

Dean of the Faculty of Health Sciences,
Trinity College Dublin

Dublin City Sport & Wellbeing Partnership

Fighting Blindness Ireland

FutureNeuro and S3 Connected Health

Health Research Board

HRB Structured Population and Health-Services
Education Programme (SPHERE)

Irish Cancer Society (ICS)

Irish Research Council (IRC)

Marie Skłodowska-Curie Actions COFUND

National Children's Research Centre

National Institutes of Health

North Dublin Home Care

Provost PhD Project Award

Science Foundation Ireland (SFI)

The Meath Foundation

Thierry Latran Foundation

John Scott Fellowship, Trinity College Dublin

The Royal City of Dublin Hospital Trust'

Viatrix Ireland

Wellcome Health Research Board ICAT

Acknowledgements

Acknowledgements

Professor Ursula Fearon
Director of Research, School of Medicine

Professor Catherine Darker
Director of Postgraduate Learning and Teaching,
School of Medicine

Ms Bridget Gavin
Research Impact Officer, School of Medicine

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September 2022



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