Thirteen HRB awards supporting researcher career development.

Seven Emerging Investigator Awards with a total value of €5.6 million.
Six Emerging Clinician Scientist awards with a total value of €6.9 million.

Awards listed by Host Institution

Trinity College Dublin

6 awards with a total value of €5.3 million

1. Lead Applicant: Dr Alison Keogh

Mobility mapping: Working with people with multiple sclerosis to map real-world walking experiences to digital mobility outcome measures, to improve clinical assessment.

Emerging Investigator Award - Patient Oriented Research
Award Amount: €725,199

Lay summary:

Changes to walking, or mobility, as a result of multiple sclerosis (MS) can impact a person's daily life, influencing many activities and altering people's sense of independence. These changes are rated as important to people with MS, however, no measures currently exist that accurately monitor people's mobility outside of a clinic or lab-based setting. This means that we currently rely on brief snapshots in time to understand how people are walking.

Measuring mobility in people's daily environments would allow researchers and clinicians to better understand the impact of MS on people's lives. Wearable devices (e.g. sensors, smartwatches, phones etc.), offer us the chance to do this, by creating new outcome measures of mobility from the data captured by them. These digital outcome measures may then be used in clinical trials in the same way that other outcome measures, such as scans, already are. This may provide us with insights into how MS symptoms are impacting a person's mobility, and, over-time, may also prove to be a valuable measure of treatment effectiveness or disease progression. The first step though is to develop them.

It is critical that a person-centred approach is taken in the development of new outcome measures, to make sure that we select and understand which outcomes are most important for people with MS. We will interview 60 people with MS, from diverse backgrounds, in multiple countries across Europe, to understand (i) how MS impacts their daily lives, and (ii) to map these experiences to the developed digital outcome measures. We will build on the results of these interviews by undertaking a consensus process with healthcare professionals to prioritise outcome measure development. This project will therefore support the development of new, patient-driven outcome measures for clinical trials in MS, by ensuring that new measures are meaningful for people.

2. Lead Applicant: Dr Gina Leisching

Targeting Thromboinflammation in Systemic Lupus Erythematosus

Emerging Investigator Award - Patient Oriented Research
Award Amount: €817,086

Lay summary:

Systemic lupus erythematosus (SLE) is an autoimmune disease marked by premature atherosclerosis (precursor to heart disease) and thrombotic (clotting) complications. The increased levels of interferon (IFN)α, which is an immune protein, is observed in SLE and worsens cardiovascular and thrombotic risks, creating a cycle of inflammation and clotting.

Therefore, the long-term goal of this project is to reduce the burden of premature atherosclerosis and thrombosis in SLE. The central hypothesis, based on my preliminary data suggests that IFNα-driven activation of 3 specific immune cells, low-density neutrophils (LDNs), normal-density neutrophils (NDNs), and macrophages lead to premature atherosclerosis and thrombosis through the altered metabolism of these cells. The project's objectives are (1) to identify distinct metabolic and inflammatory profiles in SLE-derived LDNs and macrophages, (2) to evaluate the role of changing metabolism in blood coagulation, and (3) to determine immune pathways linked to clotting in SLE. This study is innovative in its (a)interdisciplinary approach to dissecting metabolic reprogramming, inflammation, and coagulation in SLE and (b)introduces a novel concept that premature atherosclerosis and thrombosis in SLE are intricately linked to metabolic alterations in LDNs, NDNs, and macrophages, which have not yet been investigated. It holds significance in identifying new therapeutic targets and providing a model approach for understanding these processes in SLE, which are potentially applicable to other chronic inflammatory conditions.

This project therefore addresses the urgent need to assess the links between immunity and coagulation, setting a pioneering milestone in this area of SLE research. This study, crafted through collaborative efforts between St.James' Hospital in Dublin and a core research team offers the promise of advancing our understanding of SLE pathogenesis and providing novel therapeutic avenues for reducing thrombotic complications in this patient population. This work will therefore contribute to building a robust and impactful research ecosystem on SLE, which is currently lacking in the Republic of Ireland.

3. Lead Applicant: Caoileann Murphy

Enhancing Wellbeing in Residential Care: a focus on Body Composition and Skeletal Muscle Function (RES-FIT)

Emerging Investigator Award - Patient Oriented Research
Award Amount: €818,880

Lay summary:

Residential care facilities play a vital role in supporting people who can no longer be cared for at home. As the number of older people in Ireland continues to grow, there is an increasing demand for these essential services. Top priorities within residential care facilities are to maintain residents' independence, ensure a good quality of life, and deliver person-centred care. While studies have identified a rise in obesity among residents, there's limited knowledge on how obesity impacts independence, health, and overall well-being. Another common concern is the development of sarcopenia, a condition resulting from the loss of muscle mass and strength, which can lead to falls, physical disability, and a diminished quality of life. When obesity and sarcopenia occur together, the consequences may be especially harmful.

Currently, there is a lack of data on the prevalence of obesity and sarcopenia in Irish residential care facilities. Our research programme aims to fill this knowledge gap across the entire country. We will investigate how obesity and sarcopenia affect the independence, quality of life and health of residents, using data collected in Ireland and other countries. Additionally, we will track individuals over time following their transition to residential care, observing changes in their bodies and the impact of these changes. We will also gather resident and staff perspectives on these changes and their underlying causes. Public and Patient Involvement (PPI) partners will work alongside our research team, shaping and guiding the project at every stage. The information generated by this collaborative research will help improve the way residential care facilities operate. It will guide decisions about things like food, physical activity, and monitoring. It will also help plan for the right number and types of staff and the design of the facilities to better serve the needs of residents

4. Lead Applicant: Dr Nicky O'Boyle

Targeting opportunistic Enterobacteriaceae in ileal Crohn's disease using D-amino acids

Emerging Investigator Award - Patient Oriented Research
Award Amount: €898,831

Lay summary:

Inflammatory bowel disease (IBD) is a long-term illness that can result in a wide variety of debilitating symptoms including diarrhoea, abdominal pain, extreme tiredness, unexplained weight loss, joint pain, skin rashes, mouth ulcers and eye irritation. Despite being a widespread problem, there is a limited availability of effective treatment options. In fact, IBD is a lifelong disease that is currently incurable. There is a strong association between flare ups of IBD and changes to gut bacteria, some of which are thought to be harmful and can overgrow and replace "healthy" bacteria. Being able to identify markers for IBD in urine or faeces is highly desirable and it has recently been shown that some forms of IBD are associated with lower levels of faecal D-amino acids (DAAs). My research has shown that these chemicals, primarily produced by bacteria, have a remarkable ability to reduce several harmful effects of E. coli bacteria. In this work, I will assess IBD patients for faecal DAA levels, and signs of microscopic gut damage caused by harmful bacteria. I will grow intestinal cells from IBD patients to create enteroids (a synthetic gut lining that closely resembles the gut of the patient). These will be infected with harmful bacteria from the same patient and treated with DAAs to look at their potential to prevent growth of the bacteria and damage to the gut lining. Additionally, some patients report flare ups of symptoms with certain foods. I will involve a patient group in the project to identify these foods and any effects of fermented foods (shown to contain high levels of DAAs) on flare ups. This work will help us to design tailored dietary interventions or food supplements that target this problematic group of bacteria.

5. Lead Applicant: Dr Antoinette O'Connor

Biomarkers in the identification of Alzheimer's Disease in people with Down Syndrome (Bio-MinDS)

Emerging Clinician Scientist Award - Clinical Research

Award Amount: €1,340,039.90

Lay summary:

Nearly every person with Down syndrome eventually develops Alzheimer's disease (AD): the hallmark proteins of AD are found in 9 out of 10 people with Down syndrome by the age of 40, and by age 65 nearly all people with Down syndrome have dementia. We are entering a new era in AD treatment– for the first time there are therapies that can slow disease progression. Frustratingly, people with Down syndrome have been routinely excluded from AD drug trials, despite urgent clinical need in this population. Therefore, we do not know if these potentially life altering treatments work in Down syndrome.

Robust clinical trials in Down syndrome will need to track AD-related change – these measures of change are called biomarkers. Biomarker selection in this population is not straight-forward: traditional measures (cerebrospinal fluid sampling and brain scans) are invasive and expensive, while variability in intellectual ability leads to challenges standardising cognitive testing. Blood tests represent an ideal AD biomarker as they are cheap, accessible and repeatable.

Before blood tests can enter routine use a number of important questions must be answered. My research will address some of these, specifically:

- what role does inflammation play in driving AD onset?
- what blood tests are the most promising for the detection of AD in Down syndrome?
- do blood test levels vary from day-to-day and does this variability impact on their ability to diagnose AD and/or track change?
- how long, and how many people, are required to participate in AD clinical trials to show a treatment effect in Down syndrome?

I will answer these questions by reviewing previous blood biomarker studies in Down syndrome and by collecting repeated blood samples from people with Down Syndrome. These blood samples will also allow me to investigate the role of inflammation in AD -potentially identifying new treatment targets.

6. Lead Applicant: Dr Gráinne Sheill

Towards an evidence based and stakeholder informed model of rehabilitation for people with haematological cancer

Emerging Clinician Scientist Awards - Clinical Research
Award Amount: €668,936.72

Lay summary:

Background

Many people with haematological (blood and lymphatic) cancer undergo a haematological stem cell transplant (HSCT). HSCT replaces damaged blood cells with healthy ones and often involves high doses of chemotherapy. Patients who receive a HSCT can experience numerous weakening side-effects, such as decreased physical performance, which negatively impact on their quality of life. Rehabilitation is widely promoted in cancer care to enhance outcomes and lessen the negative impact of treatment; however it is unclear how rehabilitation is best provided to support patients receiving intense treatments like HSCT.

What question am I asking?

What is the impact of HSCT on physical wellbeing and what are the best rehabilitation approaches to supporting patients to recover after HSCT?

How will I answer this question?

This study involves three work packages. Work Package 1 will combine the results of published studies where patients describe their experience of undergoing hematopoietic stem cell transplant. The findings of individual studies will be drawn together to give greater understanding of the rehabilitation needs of patients undergoing HSCT.

Work Package 2 will evaluate the effects of treatment on physical health. Patients will complete tests examining physical performance and questionnaires capturing patient-reported outcomes at regular intervals throughout their treatment journey (from diagnosis up to 1-year after transplant). This study will also explore if patient characteristics (e.g. fitness, age) can affect outcomes (how that person tolerates cancer treatment).

Work Package 3 will use experience-based co-design to develop a rehabilitation intervention that meets the needs of patients undergoing HSCT. Experience-based co-design is a method for helping patients and clinicians work together to improve healthcare services. Patients, carers and staff will be invited to attend interviews and codesign sessions.

Together, this study will determine the impact of treatment on the physical performance of patients undergoing HSCT and develop a rehabilitation programme to address patient's needs.

University College Cork

2 awards total value: €2 million

1. Lead Applicant: Dr Elaine Mc Mahon

Targeting inequalities in self-harm and suicide among children, adolescents and young adults (EQUALISE)

Emerging Investigator Award - Public health research
Award Amount: €695,251

Lay summary:

The issue of self-harm in children, adolescents and young adults is of increasing concern. In Ireland we have seen an increase in rates of young people going to hospital having harmed themselves. Youth suicide is also an issue of concern and is strongly linked to having previously self-harmed. The COVID-19 pandemic had a particularly severe impact on the mental health of young people, with further research needed to fully understand this. Researchers have reported that inequalities such as deprivation, poor education and poor housing all have an impact on the risk of suicidal behaviour, as well as mental health factors, substance use and adverse events. However, the role of inequality has not been reflected in the design policies to reduce suicide.

The proposed research programme will examine how social determinants including gender, ethnicity, income, housing and education affect suicidal behaviours through several inter-linked national studies. The first study will examine the inequalities underlying youth suicide through a study which collected data on all suicides in a five-year period in Ireland. Groups at high risk of suicide will be identified through comparison of the people who died by suicide with general population statistics. The second study involves a large-scale survey of young people, carried out during and after the COVID pandemic, to identify the key social determinants of attempted suicide and suicidal ideation, examining factors such as access to healthcare and mental health factors. Finally, the ways in which childhood deprivation may lead to self-harm in young people through other factors in early adolescence such as substance use or adverse events, will be explored in the third study. In order to make practical impacts on youth suicide prevention policies and mental health services, researchers and experts will identify and prioritise policy approaches to reduce the inequalities impacting youth suicide risk.

2. Lead Applicant: Dr Sarah Moran

A window into glomerular inflammation - the predictive biomarkers in glomerular diseases.

Emerging Clinician Scientist Award - Clinical Research

Award Amount: €1,356,031

Lay summary:

What is the Problem We Are Trying to Address?

Glomerulonephritis (GN) is a leading cause of kidney failure around the world, leading to premature death and increased health care costs. ANCA-associated vasculitis (AAV) is a leading cause of kidney failure from GN.

GN can affect the filters (glomeruli) inside our kidneys, whose function is to clear toxins from our bodies. GN can lead to scarring of these filters which can cause kidney failure. Treatments include forms of chemotherapy. Kidney biopsies are used to diagnose these conditions. However, after diagnosis there is a gap our knowledge of how we monitor patients. Repeat biopsies are not usually performed due to bleeding, pain and costs. A non-invasive test, such as a urine test could allow us to monitor what is occurring within the kidney in a repetitive, safe and painless way. This research group has developed a urine test measuring kidney inflammation (sCD163) but further study is needed.

What are we proposing?

To use urine tests of inflammation in vasculitis and other forms of GN to understand who will develop kidney failure, not respond to conventional treatment and who has entered disease remission.

How will this help patients?

This project will allow us to understand the clinical utility of safe, painless urine tests in monitoring patients with inflammatory kidney disease. These tests will help inform our patients and their clinical team of their personal risk of kidney inflammation and failure, therefore allowing an opportunity to potentially intensify treatment to attempt to stop the decline in kidney function. These urine tests may help reassure those at low risk of kidney failure and potentially allow for a reduction in treatments.

RCSI University of Medicine and Health Sciences

3 awards total value: €3 million

1. *Lead Applicant: Dr Mark Murphy*

Targeting New Therapies for Alpha-1 Antitrypsin Deficiency by Linking Cellular Stress and Lung Immune Cell Outcomes

Emerging Investigator Award - Patient Oriented Research
Award Amount: €814,146

Lay summary:

This study will look at the causes of chronic obstructive pulmonary disease (COPD) in the rare disease Alpha-1 Antitrypsin Deficiency (AATD). People with AATD generally develop COPD before middle age, even if they don't smoke. There are few effective therapies for this condition. One treatment option is to increase levels of AAT but this does not stop the loss of lung function in patients. This loss of lung function is most likely due to the cells of the lung not working properly and may be caused by 1) a build-up of misfolded AAT protein in the cells, and/or 2) the effects of inflammation due to loss of the AAT protein. This may lead to cell death or senescence, where cells don't die but stop dividing, which others have shown in the liver in AATD and our own early data shows also takes place in the lungs in AATD.

Importantly, this study will look at the possibility of targeting these causes as a potential therapy. Using a preclinical mouse model of the disease we will look at the effect of loss of AAT protein on cell death and senescence and also the levels of lung inflammation. We will also look at the potential of a group of drugs called senolytics to treat the condition. These drugs remove senescent cells and we will look at the effect of this on lung inflammation.

This study will provide new insights into what causes lung disease in AATD-COPD and it will also test two novel therapies in a model of AATD for the first time. Ultimately, this study will reveal whether anti-senescence therapy will be beneficial in preserving the lung function of people with AATD worldwide over decades of their lives.

2. Lead Applicant: Dr Imran Sulaiman

Active lower airways dysbiosis with smoke exposure leads to physiological impairment consistent with chronic obstructive pulmonary disease

Emerging Clinician Scientist Award - Clinical Research
Award Amount: €1,270,856.70

Lay summary:

Chronic obstructive pulmonary disease (COPD) is a big problem in Ireland and worldwide. It happens when the airways in your lungs get inflamed over time, making it harder to breathe. People with COPD often feel very short of breath, cough a lot, and get chest infections often. This really affects their life quality. There's no cure for COPD, and we don't have treatments that can stop it from getting worse or make people live longer. While smoking is a common cause of COPD, not everyone who smokes develops COPD.

To better understand COPD and find new treatments, researchers are exploring new technologies. One exciting field of study is the lung microbiome. This includes all infectious organisms like bacteria, viruses, and fungus in your lungs. Some studies suggest that some of these micro-organisms might in fact make COPD worse and cause more infections. However, we are still not fully sure what these organisms do in the lung and how they might lead to the development of COPD.

After discussion with patient advocacy groups as well as patients, and identifying patient priorities, we have come up with the following proposal. Through this study, we want to evaluate patients who have smoked a lot, some with COPD and some without. We'll collect different sample types including some from their lungs through a routinely performed camera test (bronchoscopy). And then use new technologies to see how the lung microbiome might be linked to early-stage COPD and what other factors might contribute to lung problems. This will thus lead to newer treatment strategies and improve the quality and safety of care for patients with COPD in Ireland.

3. Lead Applicant: Ms Roisin Dolan

Use of sentinel skin flap vascularised composite allograft for real time immuno-monitoring and early identification of acute rejection in highly sensitised renal transplantation recipients.

Emerging Clinician Scientist Award - Clinical Research
Award Amount: €982,028.41

Lay summary:

The major causes of kidney transplant loss are immunological. A kidney transplant is indicated when a patient suffers from irreversible kidney damage. Some patients (who have had blood transfusions, pregnancy or a transplant in the past) are at higher risk of rejecting their new kidney. Rejection is reduced by immunosuppression medication that dampens the body's immune system. The sooner rejection is detected and treated, the less damage is sustained by the organ.

We have discovered a new technique that (a) may permit a more rapid detection of rejection, permitting early treatment and preventing organ injury and (b) reduces the likelihood of rejection by changing how the immune system responds to the new kidney. The technique is called a sentinel skin flap (SSF). This involves transplanting a small patch of skin (eye-shaped and the size of two fingers together) from the same donor onto the forearm of the patient at the same time they receive the kidney transplant. If rejection develops, a rash appears on the skin. Rejection is treated as soon as the rash appears, to prevent the organ also rejecting. This could potentially reduce the immunosuppression drug levels and the side effects of these, and avoid rejection injury to the kidney.

We will transplant a skin patch along with the kidney and take samples to monitor the immune response in detail during the first year. This is particularly beneficial if there are rejection events, to find out if and why the skin flap is beneficial in combination with a kidney transplant.

University College Dublin

2 awards total value: €798,7222 awards total value: €2.2 million

1. Lead Applicant: Dr Kieran Brennan

Blood based-liquid biopsy for prediction of Immunotherapy response in Multiple Myeloma

Emerging Investigator Award - Patient Oriented Research

Award Amount: €798,722

Lay summary:

Multiple myeloma is a blood cancer that arises due to excessive growth of plasma cells in blood and bone marrow. The plasma cells circulate between the blood and bone marrow, and send signals to promote myeloma progression. One signal type sent by myeloma cells occurs via the release of small spherical vesicles known as extracellular vesicles (EVs), that contain functional contents of the myeloma cell. Released EVs are taken up by other cells and alter cell function. Thus, the released EVs act as a surrogate marker of the cell from which they were released. EVs are highly abundant in body fluids including blood, bone marrow, saliva and urine, making them easily accessible means of monitoring myeloma in real time. This approach has many advantages over invasive bone marrow aspirate that is currently used for myeloma monitoring.

This project is focussed on monitoring the EV levels of a combination of proteins that are involved in the development of resistance to the myeloma therapy known as Daratumumab (Daralex). We previously found that these proteins are detectable on the EVs present in the blood of myeloma patients undergoing Daralex treatment. In this proposal we will monitor these proteins on EVs from MM patients before and during Daralex therapy to determine how levels change and how the pattern reflects response to treatment. We will also use advanced technologies to identify additional contents of EVs that differ between patient that respond or don't respond to treatment. Overall, we aim to develop a non-invasive blood test to monitor myeloma progression over the course of treatment that can be used to predict therapy response, thereby aiding clinical decisions on an individual patient basis.

Lead Applicant: Associate Professor Tomás Barry

Project: Intelligent and innovative planning for community based unscheduled care

Health Services Research

Award Amount: €1,396,425.30

2. Lead Applicant: Associate Professor Tomás Barry

Intelligent and innovative planning for community based unscheduled care

Emerging Clinician Scientist Award - Health Services Research
Award Amount: €1,396,425.30

Lay summary:

Research focus

This research will focus on GP (general practice) and Paramedic based 'unscheduled care' services. Unscheduled care is healthcare which cannot be foreseen in advance. This is why unscheduled care must be available 24 hours a day, 7 days of the week.

Why is this important

Ireland's population is growing and getting older. This means that the demand for health services including unscheduled care is increasing dramatically. At the same time there is a growing shortage of healthcare professionals in Ireland and across the world. Increasingly, healthcare services are trying to move away from hospital care into the community. Care in the community is considered more cost efficient and may be preferred by patients as it is closer to home. When the right type of GP and Ambulance/Paramedic unscheduled care services are available this can ensure patients do not need to travel to or be admitted to hospital for treatment. Health professionals are more likely to want to work in services that are innovative, and more responsive to patient's needs.

What we propose to do

We wish to produce a plan to guide the evaluation of integrated GP and Paramedic unscheduled care services that are being developed in Ireland and internationally.

How we propose to do it

We will produce this plan by working with key stakeholders including clinicians, patient representatives and health-service managers to conduct this research. We will use the latest available statistical technology to analyse data about the population, the location of health services and current unscheduled care usage patterns. We will then model future demand for unscheduled care based on Ireland's changing population. We will consult with patients, service providers and international experts to develop a framework that can be used to evaluate novel initiatives where paramedics and GPs work together to deliver unscheduled care.