

School of Medicine **Research Strategy** 2021-2026



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

“The connection to clinical translation inspires our researchers to provide improved insight and enhanced solutions that can benefit patients, health professionals and the broader health system in Ireland.”



Contents

Foreword	05
Research Strengths and Infrastructures	07
Research Vision and Values	13
Research Mission	14
Research Strategy Plan at a glance	15
Pillar 1: Engage in excellent research and promote cutting edge innovation	16
Pillar 2: Invest in people and infrastructures	18
Pillar 3: Expand research opportunities and success	20
Pillar 4: Communicate impact and societal outreach	22
<hr/>	
Research Impact Stories	
Gene therapy for haemophilia offers a potential cure	29
The best model of human disease is the human	30
Tripartite alliance to battle COVID-19	31
Building international research into a rare autoimmune disease around a registry and biobank	32
The KARMA-Dep-2 trial: Ketamine as a treatment for major depression	33
Energy to burn – how immune cells respond to infection during TB disease	34
An innovative method for detecting frailty	35
Cancer immunotherapy as a first-line treatment	36
Pushing boundaries on Alzheimer's detection, prevention, cure and care	37
The Irish childhood national diabetes register	38
Research on ageing: From research to practice to policy	39
Exercise is key following a cancer diagnosis	40
A 'one-stop' health surveillance clinic for children with Down Syndrome	41
Cellular biomarkers of disease onset, progression and response to treatment for rheumatoid arthritis	42
A new method of measuring satiety in clinical trials of hyperphagia and obesity	43
Pioneering international research into transforming health systems	44
Better ways to tell our story	45
<hr/>	
Acknowledgements	46

“Together with key stakeholders, we will co-create our research questions and define outcomes that are truly meaningful.”



Foreword

The Trinity College School of Medicine is a vibrant research-led school with strong clinical academic partnerships and an international perspective. The connection to clinical translation inspires our researchers to provide improved insight and enhanced solutions that can benefit patients, health professionals and the broader health system in Ireland. Our international collaborations help to drive the excellence for which our researchers are known.

In a rapidly changing world, we are facing many new health challenges. Our researchers showed great agility in adapting their research to meet the immediate challenges of the global pandemic. However, many new challenges will persist long beyond the pandemic, such as the impact on ageing, mental health, climate change and obesity.

In the context of these health challenges, we are delighted to present the School of Medicine Research Strategy 2021-2026. Together with our academic partners and

our research institutes, we will combine our clinical expertise with new tools, technologies and big data that will be transformative for healthcare. We will do this through strategic investments in infrastructures and by expanding our collaborations within Trinity

“We will combine our clinical expertise with new tools, technologies and big data that will be transformative for healthcare.”

Professor Louise Gallagher
Director of Research

College Dublin and beyond. We will leverage sufficient investment through exchequer and non-exchequer funding and by giving our researchers the supports that they need to succeed. The actions planned under the key priority areas are ambitious but achievable and, as they are implemented, will collectively

enable the School to deliver significant impacts on national and international healthcare developments.

Our research will be embedded within a framework of demonstrating impacts that go beyond conventional metrics. Together with key stakeholders, we will co-create our research questions and define outcomes that are truly meaningful.

It was a pleasure to work with the School of Medicine Research Committee, the School of Medicine Management Team and other colleagues across the School in the development of this plan. I am grateful to them and to the team that produced this plan. I look forward to seeing our research success grow and have a measurable impact over the next four years.

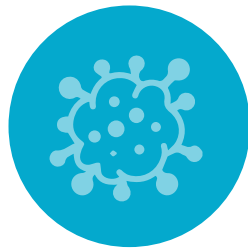
Professor Louise Gallagher
Director of Research
School of Medicine 2019-2021

School Research Strengths

Improving human health and healthcare from bench to bedside across traditional and emerging research areas



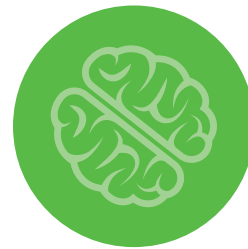
**Children's
Health**



Cancer



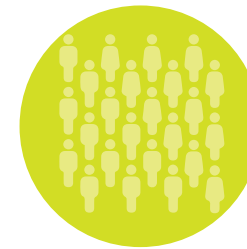
**Personalised
Medicine**



**Mental Health
and
Neuroscience**



**Infection &
Immunology**



**Population
Health and
Health Policy**



Ageing

Scale of Research at School of Medicine



The School of Medicine is Ireland’s leading medical school and ranks as one of the world’s top medical schools (2021 QS world rankings 100-150). The School of Medicine is the leading research school in Trinity, home to over 800 highly diverse researchers and spanning 21 medical and scientific disciplines. The School of Medicine is a multidisciplinary school comprising Medicine, Radiation Therapy, Occupational Therapy, Physiotherapy, Human Health and Disease, and Human Nutrition and Dietetics. Over 90% of the academic staff are

highly active in research. Fifty per cent of senior principal investigators are clinical academics

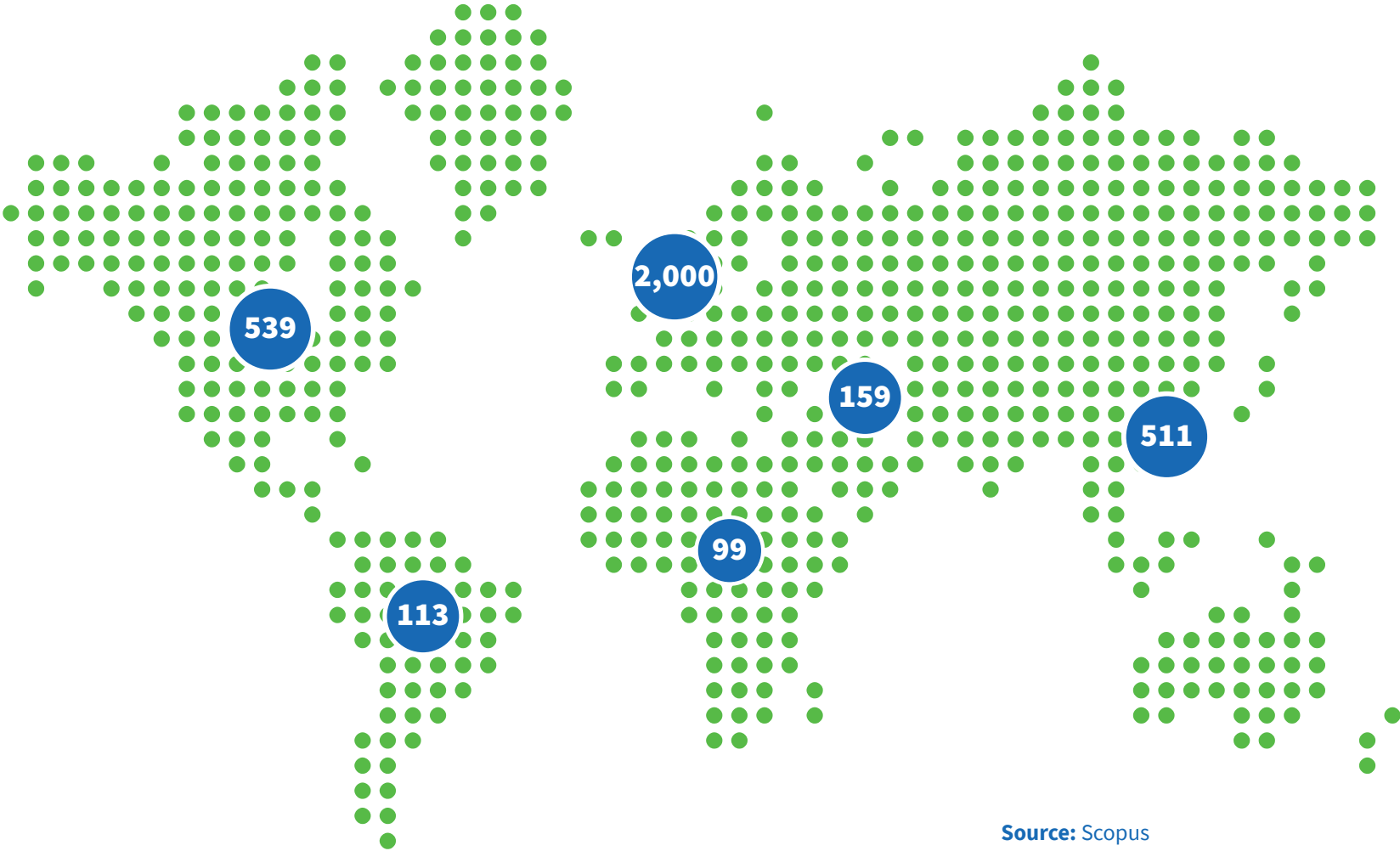
“50% of senior principal investigators are clinical academics combining their clinical commitments with their academic activities.”

combining their clinical commitments with their academic activities.

The School of Medicine research income comprises around one-fifth of the total research income of Trinity College Dublin. We are a research-led school that values cutting-edge innovation and leverages local, national and international collaboration. Multidisciplinary is one of our great strengths. Partnerships between our researchers and clinicians generate unique synergies to advance basic and translational research at every stage of the life-cycle.

Global Collaborations in Health Research 2021

Figure 1. Number of International Academic Collaborating Institutions, by region

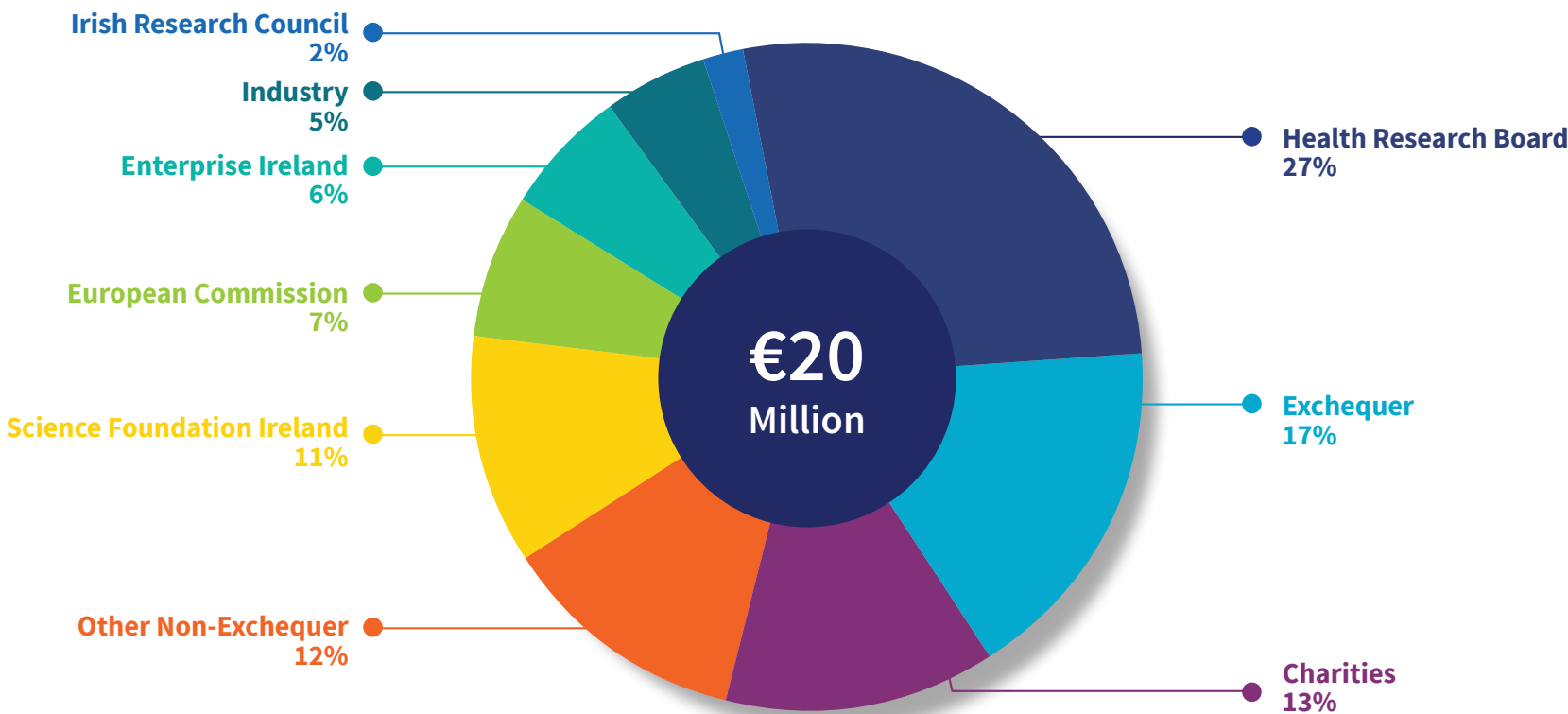


Source: Scopus

Research Funding

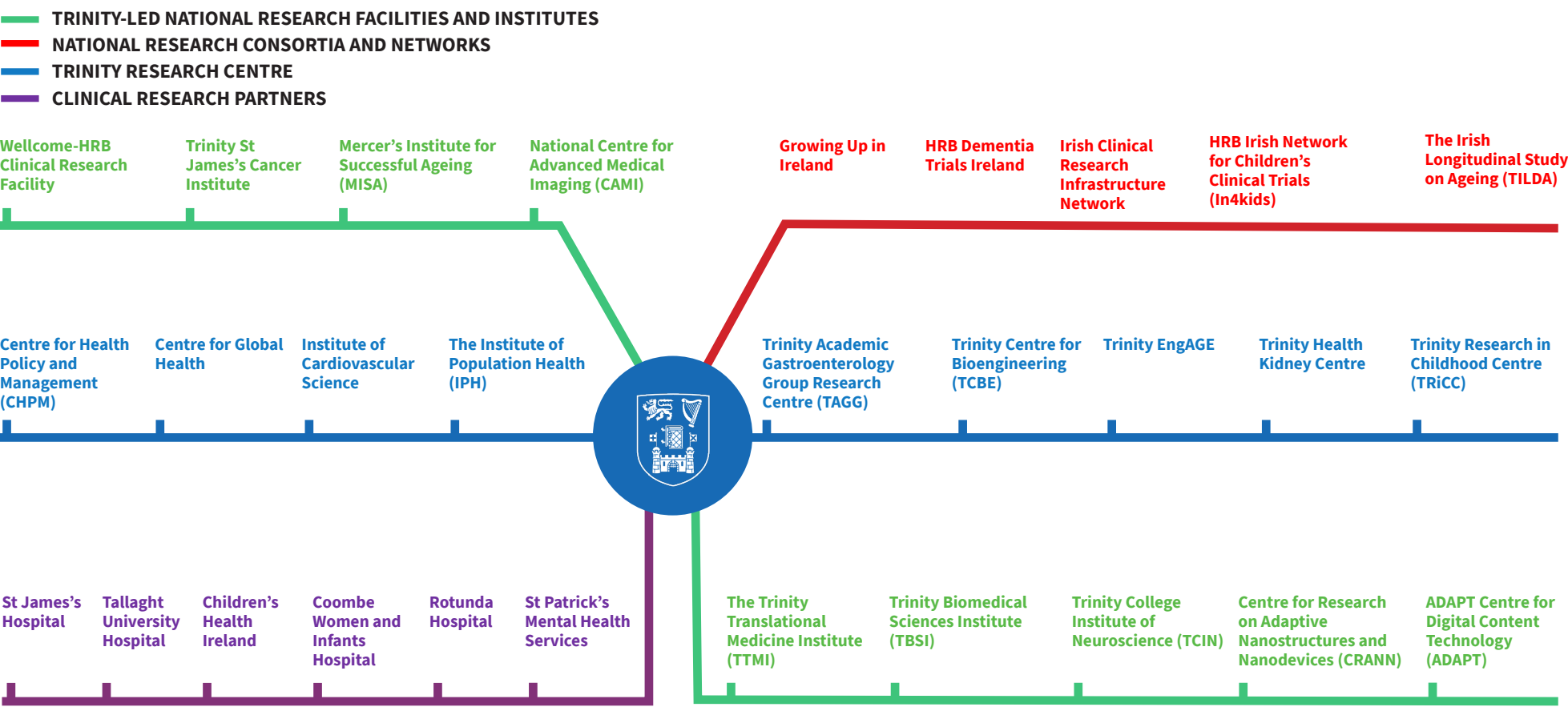
Historically, 40% of School of Medicine research income has been drawn down from Health Research Board (HRB), with Science Foundation Ireland (SFI), accounting for 20-25% of the total research income. With the average amount of grants falling and the SFI funding envelope tightening, we will need to diversify funding avenues so that income continues to grow.

Figure 2. School of Medicine Research Income 2020



Research Infrastructure and Connections

Figure 3. School of Medicine Academic and Clinical Connections, by research sector



Research Infrastructure and Connections

The School's research activities are enriched by its complex and dynamic web of collaborations with research institutes, research centres, national research consortia and networks, other Trinity schools, and hospital and health service partners.

The School is closely associated with the Trinity Translational Medicine Institute, the Trinity Biomedical Sciences Institute, the Trinity College Institute of Neurosciences, and the Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN), as well as large research and training programmes, such as TILDA, AMBER, the Global Brain Health Initiative and the Wellcome-HRB Clinical Research Facility at St James's Hospital.

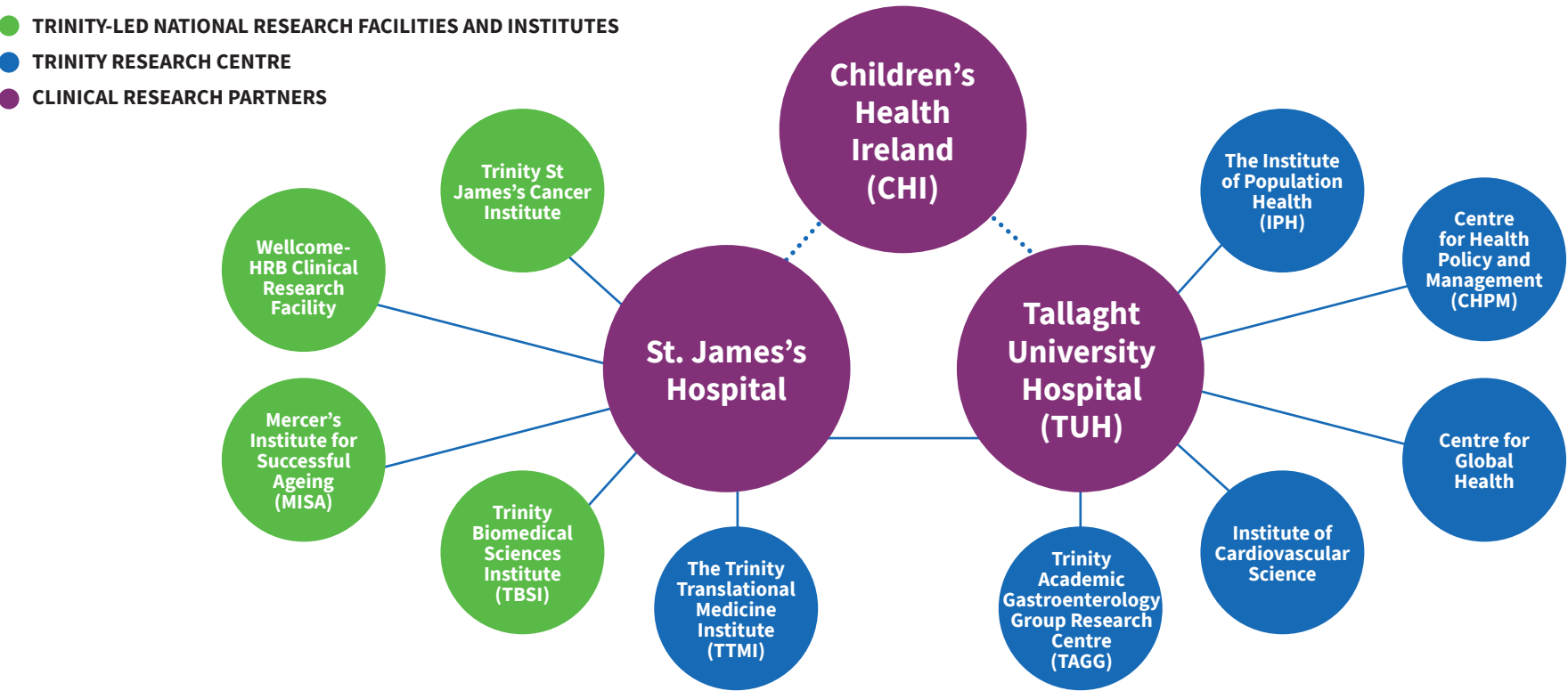


Synergies with Hospital Partners

The multidisciplinary nature and scale of the research and educational activity in the School, where Trinity researchers work in partnership with clinicians in teaching hospitals and healthcare partners, generates a unique synergy which advances basic and translational research at every stage of human life.

A key challenge of the new strategy is to encompass the vast complexity and breadth of the research undertaken at both the micro and macro levels, as well as reflecting the national and international context in which the School operates.

Figure 4. Key Synergies between Research Facilities and Hospital Partners



Research Vision and Values



Our research vision

School of Medicine research will be internationally respected and will lead transformation at the heart of Irish health innovation, delivering improvements in health services and patient care.

School of Medicine research will improve good health and wellbeing, as articulated in the UN Sustainable Development Goals.



Our research values

We are a research-led school that values cutting-edge innovation, leverages local, national and international collaboration, and is focused on improving human health and healthcare. We believe that this can be achieved through a blend of curiosity-driven and theme-focused strategies that address both fundamental biological questions and health inequities. All our research is performed with the highest integrity and ethical values.

We value the contributions of stakeholders, patient groups, health NGOs and the public to guide and co-design our research towards meaningful impact.

Research Mission



Support excellent and impactful research to improve health and patient outcomes.



Train the health research leaders of tomorrow.



Attract and grow an innovative and diverse multidisciplinary faculty.

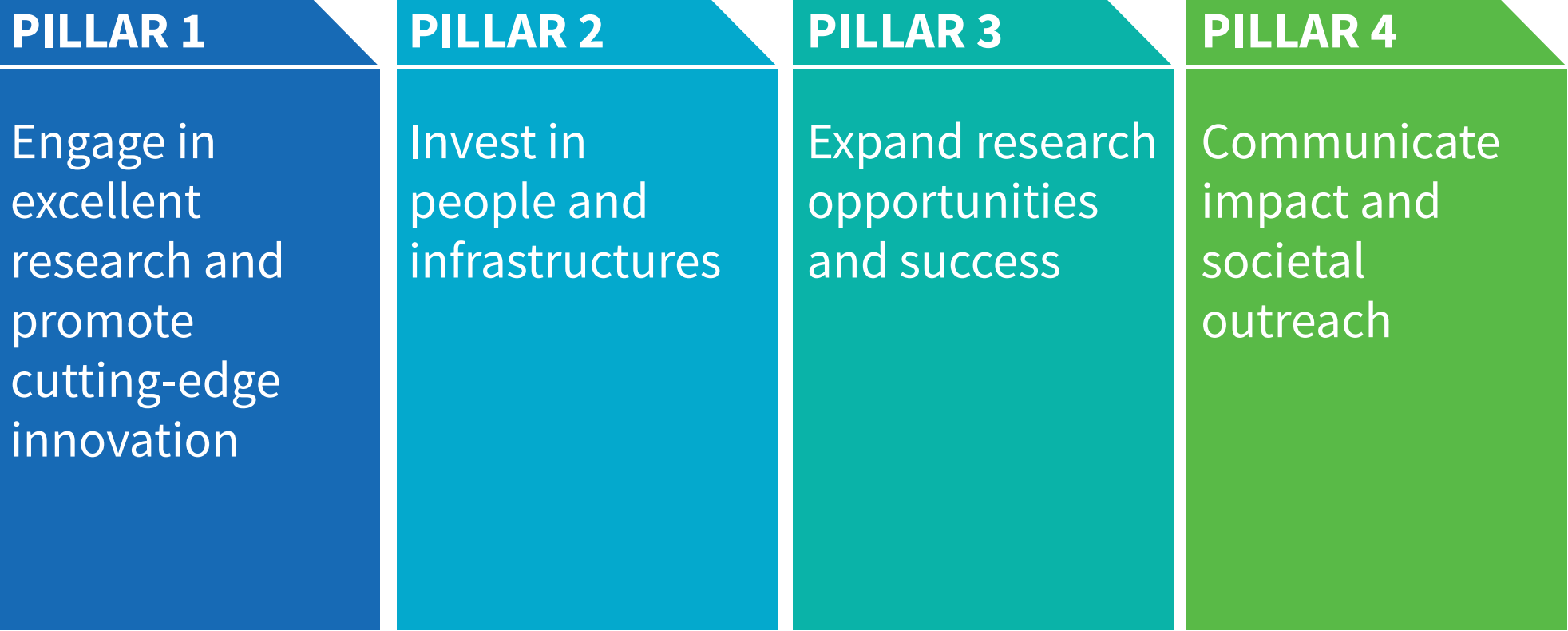


Invest in the sustainability of our infrastructures: diversify our funding.



Collaborate with all our stakeholders, including patients, to guide more meaningful impact.

Our Research Strategic Plan 2021-2026



PILLAR 1

Engage in excellent research and promote cutting-edge innovation

Our ambition is to face future global health challenges such as child health, ageing, cancer, global health threats, mental ill-health, weak health systems and health policy. It is also to face the challenges to health and wellbeing posed by climate change.

Strategic Research Pillar 1

In the next five years, we will capitalise on our strengths, on our creative and innovative faculty, and on new funding opportunities in order to increase the impact of our research.

“We will focus on our existing and emerging strategic research strengths.”

We will support our researchers to engage in excellent and impactful research that adheres to the highest standards of ethics and research integrity, and to pursue greater innovation and entrepreneurship. We will focus on our existing and emerging strategic research strengths.

Our researchers and clinicians will lead national and international research activities of impact in these strategic areas and will improve healthcare outcomes for patients and their families. We will build our activities through strong relationships between our research institutes, clinical research facility and clinical partners at St James’s Hospital and Tallaght University Hospital, and all our allied clinical partners.

PILLAR 1**ACTIONS**

Engage in excellent research and promote cutting-edge innovation



Work to provide additional resources for clinical research and secure sponsorship and legal and financial supports for our Clinical Research Facility and the Cancer Institute in collaboration with Trinity Research and Innovation.



Create and fill the position of Associate Director for Clinical Research. This post-holder will work on developing strategic plans and memorandums of understanding (MoUs) for clinical research across our clinical partners.



Seek philanthropic investment for biobanking, data management and storage infrastructures towards the development of a bioinformatics centre in TTMI.



Establish a paediatric health research subcommittee, reporting to the Director of Research.



Develop a strategy for paediatric health research at Trinity which will serve as a key contact point for research developments related to Children's Health Ireland.



Appoint an Associate Director for Research Integrity, Ethics and Open Scholarship to create clear policies and guidelines on research integrity, ethics, data protection and governance.

PILLAR 2

Invest in
people and
infrastructures

A diverse and innovative faculty is core to our research mission. We recognise the contributions of researchers at every stage of the research trajectory and the necessity for a viable and sustainable career pathway.

Strategic Research Pillar 2

Strategic hires are required to provide necessary expertise in biostatistics and bioinformatics to prepare our researchers to take on the challenges of bioinformatics and

“We will support the development of clinician scientists and the health research leaders of tomorrow.”

data analytics in medicine. We will attract world leaders through prestigious schemes such as the SFI research professorships, European Research Council, Wellcome Trust and Health Research Board.

We will prioritise research areas for future Trinity assistant professorship schemes to provide career progression for our early- to mid-career researchers, and will support the development of clinician scientists and the health research leaders of tomorrow through better definition of the roles of clinical lectureships.

PILLAR 2

ACTIONS

Invest in people and infrastructures



Appoint a world-leading SFI research professor in a strategic research area.



Appoint an internationally recognised chair in biostatistics by 2022, who will lead the development of a biostatistics unit.



Work in collaboration with Children's Health Ireland (CHI) to identify key positions aligned with our research interests in paediatrics and child health.



Increase research-focused clinical academic training positions and new tenure-track basic science pathways, similar to the USSHER Assistant Professorship.



Establish annual prizes that recognise outstanding contributions to research and the achievements of our early-career researchers and post-graduate students.



Upscale investment in biobanking, storage and biocomputing, genomics, flow cytometry, neuroimaging and microscopy through philanthropy and strategic funding initiatives.

PILLAR 3

Expand research opportunities and success

We aim to build on our excellent high-quality research and funding track record to date as Ireland's leading medical school. Strategically we have aligned our funding objectives to the future vision and investment made by the European Commission and national and international funding agencies.

Strategic Research Pillar 3

Securing continuous improvement and breakthroughs in patients' health through their life course is at the centre of our School's investment in research and innovation within

"We will expand our international funding track record as Ireland's leading medical school."

and beyond the context of the current global pandemic crisis.

By promoting early dialogue between entrepreneurs and innovators, clinical and

biomedical researchers and the medical and healthcare industry, the School will accelerate the impact of its translational and highly technologically driven research with a view to achieving sustainability, impact and climate-neutral content. This objective will provide the opportunity to apply for Enterprise Ireland (EI) funds and several schemes under EU Horizon Europe (e.g., European 4Health, Digital Europe Programme (DEP), InvestEU, European Regional Development Fund (ERDF), European Social Fund (ESF+), Structural Reform Support Programme (SRSP) funding schemes, and Innovative Europe Pillar).

PILLAR 3**ACTIONS**

Expand research opportunities and success



Accelerate the translational impact of our research with frequent brokerage and showcasing events between entrepreneurs, innovators and clinical and biomedical researchers in the medical and healthcare industries.



Host quarterly training, information and mentoring workshops to inspire our researchers to secure prestigious funding through Science Foundation Ireland, the European Research Council, Wellcome Trust, the Health Research Board and global charities and foundations.



Continue to support our early-career researchers to successfully develop their research and professional careers, to develop their research profiles and to showcase their achievements.



Build a substantive relationship with Trinity Development and Alumni to amplify our achievements and pivot funding towards impactful research.



Extend the School's translational and multidisciplinary innovative research environments through engagement across several international and European-funded research networks.



Seek funding and collaborations from international, national and local health services to partner on, pilot and evaluate service, system and policy innovations.

PILLAR 4

Communicate
impact and
societal outreach

Research impact is how our research benefits patients, the public and broader society. Our challenge is to better measure and articulate our impact across the translational research spectrum.

Strategic Research Pillar 4

Societal outreach and communication of our impact is the cornerstone of our research communication strategy. Key to the successful implementation of improved research

“The Research Impact Officer will build capacity to measure and communicate our School of Medicine research impacts.”

communications will be the development of new processes to explore, define, capture

and communicate our research achievements that broadly reflect the societal impact of our health research, within and beyond academia.

The School of Medicine Research Impact Officer, a key role embedded jointly in the TCD Research Impact Unit and the School of Medicine, will build capacity to measure and communicate our School of Medicine research impacts.

PILLAR 4**ACTIONS****Communicate impact and societal outreach**

Develop a School of Medicine research communications plan that strategically targets our key audiences, stakeholders and communication channels.



Optimise the reach and impact of the School's communication strategy, in co-ordination with the Director of Health Policy and Impact, Office of the Dean of Research, the PPI Ignite Office and the Trinity College Dublin Public Affairs and Communications (PAC) team.



Promote and disseminate the scale and scope of our research impact through qualitative and quantitative research performance reports, impact case studies and the School of Medicine research metrics book.




Cultivate a culture of communicating our health research impacts through showcasing projects that are making demonstrable positive differences to the health and wellbeing of individuals, the community and society.



Train and support our researchers to engage with knowledge users in framing research questions and approaches. This will help to develop the work in ways most likely to lead to impact.

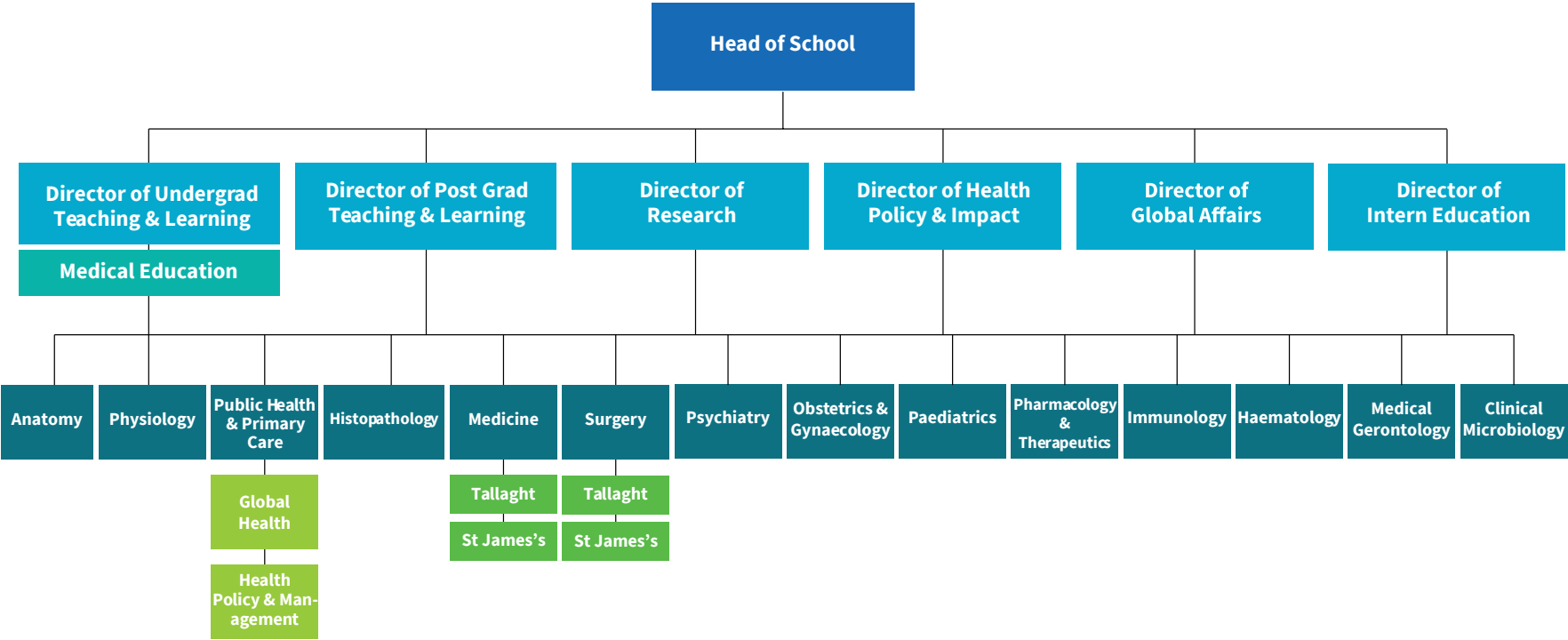


Qualitatively and quantitatively evaluate our ability to set the policy agenda; decide how issues are framed, perceived and represented in public documents and presentations; and have a definitive influence on policy.



“We will support and mentor our researchers to engage in excellent and impactful research.”

School of Medicine Research Governance



The School of Medicine Research Directorate is committed to maintaining high standards of governance and reporting and has put in place the appropriate structures consistent with this objective. Reporting lines for the Director of Research within the School and overall college

structure are clearly defined and in place. This has allowed for School involvement in decision-making processes at school and college level. The Director of Research reports directly to the Head of School and provides information to the School Executive Committee and the School

Management Committees. The Director of Research is a member of the College Research Committee, an academic committee which reports directly to Council.

Strategy Development

The School of Medicine Research Strategy 2021-2026 replaces the research strategy section of the School of Medicine Strategic Plan 2015-2019. The new strategy has been designed and agreed following a detailed and inclusive consultation process undertaken between March 2019 and March 2021. The Director of Research, Professor Louise

Gallagher, in partnership with the School of Medicine Research Committee, oversaw the project. Substantial input was also received from the School Executive Committee and the senior management team in the School.

A fundamental objective of the document is to formulate a new strategy aligned to Trinity

research strategy in the context of the Irish university system and funding environment over the next five years.

To underpin the strategy, the School undertook a comprehensive SWOT analysis, which has served as an important and valuable source of information and data to inform the strategy.



Strategy Development

The new strategy involved a detailed bottom-up and top-down consultation process, from the level of School Executive Committee right down to the individual researcher in each of the

24 disciplines. The results of the SWOT analysis provided an important and valuable source of information and data for the development of the strategy.

A distillation of the SWOT analysis produced the following key issues to address over the next five years and beyond:

STRENGTHS

- Research reputation, especially in immunology, ageing and neurology
- Emerging areas: infection, public health and epidemiology
- Cancer Institute, CRF, Children’s Hospital
- Clinical partners and hospital network

WEAKNESSES

- Bureaucracy of research financial accounting and HR processes
- Government research spend declining and average value of grants decreasing
- Lack of benchmarking of research impact and performance
- Weak communication of research output and impact
- Average size of grants decreasing

OPPORTUNITIES

- Cancer Institute
- Children’s Health Ireland
- Clinical Research Facility
- Alliances with health partners
- Opportunities for clinical research
- Clinical researchers – adjuncts, clinical lecturer posts
- Targeting specific themed calls

THREATS

- Teaching and clinical research staff work overload and pressure to obtain grants
- Falling rankings
- Limited availability of overheads for strategic investment in infrastructure
- Government research spend declining
- Heavily reliant on the exchequer for funding (SFI & HRB)

Research Impact Stories

How our researchers are making a positive impact on the health and wellbeing of the community



Gene therapy for haemophilia offers a potential cure

Haemophilia is a group of inherited disorders in which blood fails to clot properly, causing longer-than-normal bleeding. It is managed with weekly injections. Researchers in St James's Hospital took part in an international clinical trial to investigate gene therapy as a cure for patients with haemophilia. In the 54 patients in the trial, the blood-clotting factor rose by an average of 36%. This gives hope that a one-time intervention can be a permanent cure.

Currently patients with haemophilia receive prophylactic weekly injections to control the frequency and severity of bleeding and prevent joint damage or death. The condition may be mild, moderate or severe, depending on clotting-factor deficiency. Bleeding may come from gums, nose and wounds, but usually occurs internally into the knee, ankle or elbow.

The principal investigator in this gene therapy trial was Dr Niamh O'Connell, Consultant Haematologist in St James's Hospital, and

it took place at the Wellcome-HRB Clinical Research Facility (CRF) there. This innovative therapy delivers the gene into the body using a virus with adapted DNA (an adeno-associated viral vector). Patients with a new 'working copy' of genes that enable clotting

"I have lived my entire life with severe haemophilia, and I wanted to see what life would be like without severe haemophilia. And it has been very pleasant."

Brian O'Mahony

Irish Haemophilia Society CEO and gene therapy trial participant

no longer need weekly injections. In the trial, three Irish patients received the gene therapy intravenously into the liver, which started to produce the missing clotting factor.

Brian O'Mahony, a study participant and CEO of the Irish Haemophilia Society, explained that the standard prophylactic replacement therapy reduces bleeding but is not ideal. On the gene therapy he received in the clinical trial, he said: "This new treatment offers the possibility of a functional cure. The need to undergo replacement therapy several times a week take its toll. For me, taking part in this trial has increased my 'head space', in that I no longer have to constantly think about managing the condition."



The best model of human disease is the human

Neurodegenerative diseases are debilitating incurable conditions that cause decline in movement, thinking and behaviour. Amyotrophic Lateral Sclerosis (ALS) accounts for up to 10,000 deaths in Europe and costs over €600 million each year in care. It occurs in midlife, mainly causing degeneration in motor pathways but also affecting thinking and behaviour. In the Academic Unit of Neurology, we have worked on ALS for the past 25 years, identifying different subtypes with various degrees of cognitive and behavioural change, and showing a link between ALS and schizophrenia. Finding that genetic factors account for about half of the risk of developing ALS, we helped discover many new genes for ALS. Two, SOD1 and C9orf72, are the target of a precision medicine-based approach toward therapy. Our early-phase gene therapy studies of C9orf72 look promising.

However, for the forms of ALS with no established genomic basis, clinical trials of

over 70 compounds have failed to demonstrate benefit despite successes in animal models.

“Our goal is to find the right drug for the right patient in the right dose, at the right time.”

Professor Orla Hardiman
Professor of Neurology, Consultant Neurologist and Leader, ALS/MND Clinical and Research Group

We adopted a new perspective. We shifted our focus from laboratory-based work to applied clinical research in patients (<https://rmn.ie/>). We study patients as individuals – their genetic makeup, key biomarkers, prior treatment, family history, environmental factors and behaviour – as these all affect how diseases progress. This in turn influences design and testing of new treatments. Within the European consortium TRICALS (www.tricals.com)

we combine insights from epidemiology, clinical assessment, family history studies, imaging, neuro-electric-signalling, genomic and biomarker datasets to investigate the causes and progression of ALS, and develop better treatments.

We focus on human disease in humans with the same scientific rigour that was applied to laboratory work and animal modelling. With colleagues at the ADAPT Centre and internationally, we process clinical data at scale, aiming to build a unique multimodal assessment of the disease for each individual and so create more effective treatments.



Tripartite alliance to battle COVID-19

Researchers at St James's Hospital, Tallaght University Hospital and Trinity College Dublin have received €7.5 million funding under Science Foundation Ireland's Strategic Partnership Programme to accelerate research into understanding SARS-CoV2 and to develop solutions to inform pandemic responsiveness and protect our communities.

Led by Professor Aideen Long, director of the Trinity Translational Medicines Institute (TTMI) and by Professor Kingston Mills, director of the Trinity Biomedical Sciences Institute (TBSI), the team brings together clinical specialists in infectious disease, immunology, intensive care medicine and respiratory medicine with immunologists from TTMI and TBSI. It is also supported by AIB and the Clinical Research Facility funded by the HRB-Wellcome Trust.

We have various projects underway, including better diagnostic methods to detect the virus and the body's response to it; differing immune

responses to infection and vaccination among different patient groups; risk factors for disease; and the development of new

“Our research initiative has the opportunity to continue to develop and inform strategy around SARS-CoV2 infection both nationally and internationally.”

Dr Niall Conlon

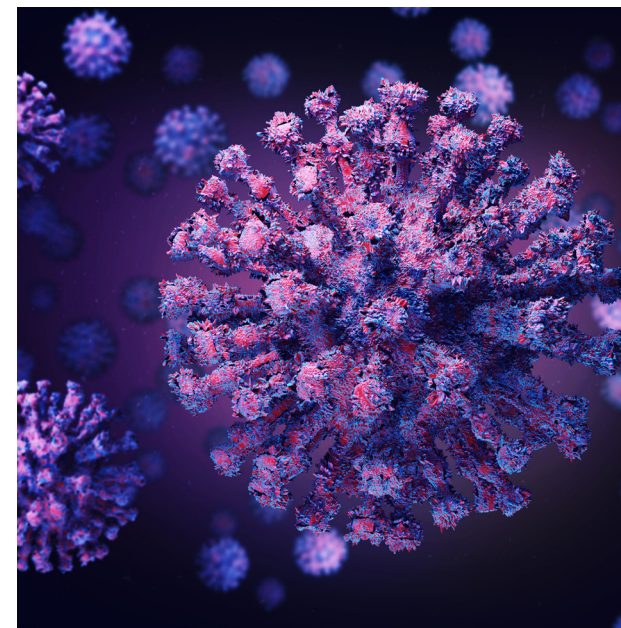
Co-chair of the STTAR Bioresource and a principal investigator on the project

treatments and improved vaccines. Significant outputs to date include:

- Developed the STTAR Bioresource, the largest COVID-19 biorepository in the country
- Introduced TriniScreen-rapid cost-effective screening for SARS-CoV2 in students and

staff at Trinity College Dublin

- Published many papers on COVID-19-related themes, including on coagulopathy, long COVID, disease severity indices and new blood tests
- Contributed to national and international COVID-19 research projects



Building international research into a rare autoimmune disease around a registry and biobank

ANCA-associated vasculitis (AAV) is a group of diseases that cause blood vessels to die. AAV is an autoimmune disease, meaning that the body's immune system targets its own healthy cells and tissue. In AAV, antibodies attack white blood cells called neutrophils, which then break through their blood vessels. This condition causes kidney and lung failure and is generally fatal if untreated. It often returns after treatment, so patients experience alternating periods of wellness and illness. Immunosuppression treatment for AAV causes serious side-effects in over 80% of patients.

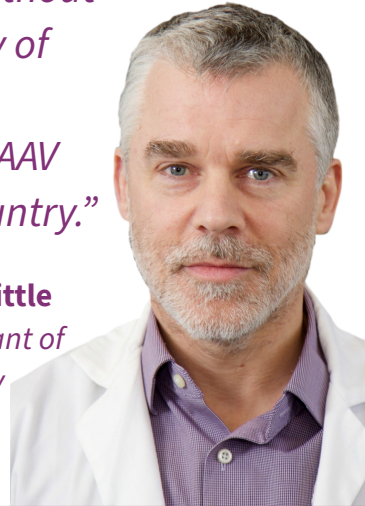
Researchers in the Trinity Health Kidney Centre identified the need for 'personalised' treatment of AAV, where doctors assess the risks and benefits of immunosuppression for individual patients. To develop this approach, we need to learn more about AAV.

Professor Mark Little founded the National Rare Kidney Disease Biobank in 2012, following

a Science Foundation Ireland President of Ireland Young Researcher award. One of the most comprehensive such databases in the world, the biobank recruited over 800 AAV

“The registry and biobank wouldn’t be possible without the generosity of nearly 1,000 patients with AAV across the country.”

Professor Mark Little
Professor/Consultant of
Nephrology, Trinity
College Dublin



patients, each with biological samples from successive stages in their medical history. This

allows us to describe the patients' progress over accurate timelines, and to link test results from their samples to clinical outcomes such as relapse, kidney failure and death. This rich resource allows the Trinity Health Kidney Centre to investigate the unmet needs of patients with AAV.

Studies from the database and biobank have supported the creation of vasculitis networks in Ireland (www.tcd.ie/medicine/thkc/vasculitis/), the UK (UKIVAS registry) and Europe (European Reference Network for rare immune disorders), and the patenting of a diagnostic kit which helps avoid invasive and dangerous kidney biopsies. The biobank has supported several Horizon 2020 projects, including the HELICAL innovative training network and FAIRVASC project, and many local Health Research Board and charity-supported projects. Thirty-one peer-reviewed publications have used data or samples from the biobank.

The KARMA-Dep-2 trial: Ketamine as a treatment for major depression

Researchers from the Department of Psychiatry at Trinity College Dublin are trialling a potential additional treatment for depression: the anaesthetic ketamine. Ketamine works differently from current antidepressants, although we are still finding out how. It may change dysfunctional brain cell pathways and connections (known as neuroplasticity). Previous studies showed it reduced depressive symptoms within one hour of single infusions, with peak effect at 24 hours.

The WHO says depression is now the leading cause of disability worldwide. For 60 years, standard pharmacological treatment has focused on monoamine neurotransmitters, such as selective serotonin re-uptake inhibitors (SSRIs). The large STAR*D study in the US found only 30% of patients achieved remission after first-line SSRI treatment and 50% after two trials. Fewer than 40% of patients had relief within 10-14 weeks.

Professor Declan McLoughlin, Research Professor of Psychiatry at Trinity, and his team at St Patrick's Mental Health Services want to see if ketamine can help people who are hospitalised with severe depression. The randomised controlled trial, Ketamine as an Adjunctive Therapy for Major Depression (2) [KARMA-Dep-2], is a definitive pragmatic trial, involving over 100 patients in real-life clinical

“Depression is the most common reason in the EU for long-term sick leave and disability.”

Professor Declan McLoughlin
*Professor of Research Psychiatry
and Consultant in Old Age Psychiatry*

settings and building on an earlier pilot. Funded by the Health Research Board, it is the first-ever clinical trial sponsored by Trinity.

The main hypothesis in KARMA-Dep-2 is that repeated ketamine infusions (twice weekly, maximum of eight infusions) alongside routine care will improve the condition of patients hospitalised with severe depression. This has never been done in Ireland before on this scale. Working with Professor Ciaran O'Neill at Queen's University Belfast, we also predict that using ketamine will reduce healthcare costs and improve quality of life. Professor Ricardo Segurado, University College Dublin, provides statistical support.



More information is available at clinicaltrials.gov clinical trials identifier NCT04939649.

Energy to burn – how immune cells respond to infection during TB disease

Tuberculosis (TB) is the most deadly infectious disease globally. About one-third of the world's population is infected with the causative agent, the bacterium *M. tuberculosis* (Mtb). Although TB is treatable and curable, it has devastating effects and the emergence of drug-resistant strains is challenging. Normal treatment includes taking several drugs for up to six months, extending to two years for multi-drug-resistant TB. By understanding how the patient (the host) and the Mtb interact, we can improve therapies which boost a patient's immune system to overcome infection. Research led by Professor Joseph Keane, Head of Clinical Medicine, Trinity and Director of the TB Service at St James's Hospital, focuses on the immune cells in the lung and how they respond when infected with Mtb.

Professor Keane's research team is based at the Trinity Translational Medicine Institute (TTMI) and works with St James's Hospital. In the lab, we infect certain lung cells (alveolar

macrophages) with Mtb and study their immune responses. One area of focus is the metabolism of immune cells. We have

“There has never been a better time to be engaged in the research of respiratory infection.”

Professor Joseph Keane

Head of Clinical Medicine

Trinity College Dublin

Director of the Tuberculosis Service

St James's Hospital

discovered how certain drugs improve the metabolism and hence the immune response of lung cells, and we are working on better ways to tackle multiple-drug-resistant TB. Such host-directed therapies can shorten treatment time, improve patient outcome and reduce costs.

Our research supports programmes in the TB service such as smoking cessation, and forms a basis for writing treatment guidelines. Professor Keane has co-authored the international CDC/ATS TB Treatment Guidelines, a globally recognised standard for TB care. Our research has been funded by many bodies, including the Health Research Board, Royal City of Dublin Hospital Trust, Medical Research Charities Group and the Irish Thoracic Society, and philanthropy.



SCHOOL OF MEDICINE RESEARCH STRATEGY 2021-2026

An innovative method for detecting frailty

Frailty is related to getting older. It describes how our bodies gradually lose their in-built reserves, leaving us vulnerable to sudden changes in health triggered by seemingly small events such as a minor infection or a change in medication or environment. Frailty brings greater risk of falls, cognitive decline and disability. It makes people more likely to need GPs, hospitals and long-term care. Our current ways of measuring frailty are not useful for detecting its early signs.

FRAILMatics is a multidisciplinary project, established in September 2020, to improve methods for detecting subtle early signs of frailty. By identifying people in the early stages and improving their resilience, we will achieve better outcomes for patients and healthcare providers. We use the latest supercomputers to analyse vast numbers of measurements of mild physiological stresses across cardiovascular, movement and brain-health systems. Analysis can show subtle but reliable signals of

vulnerability. The study will help us develop medical devices to identify frailty at an early stage.

“More accurate and earlier detection of frailty will help doctors care better for older patients.”

Professor Roman Romero-Ortuno

*Associate Professor and Consultant Physician,
Discipline of Medical Gerontology, School of
Medicine, Trinity College Dublin*

FRAILMatics will use data spanning 10 years from more than 8,000 participants aged over 50 in The Irish Longitudinal Study on Ageing (TILDA). The data will help us develop new diagnostic models, as current studies show they successfully predict frailty status, cognitive performance and biological ‘brain age’. These models will be tested and validated

on patients at Mercer’s Institute for Successful Ageing (MISA) in St James’s Hospital, Dublin. FRAILMatics will advance the science of frailty and achieve considerable savings by reducing avoidable health complications.



Cancer immunotherapy as a first-line treatment

Oesophageal cancer cases exceeded 600,000 in 2020, with over half a million deaths, making it the 6th leading cause of cancer-related mortality worldwide. In Ireland, incidence is expected to increase by 103% in males and 60% in females by 2045. Despite improvements in treatment, five-year survival rates are approximately 20%. Many urgent unmet clinical needs remain, including identifying the best treatment options; understanding the central role of the immune system; early detection through symptom awareness and screening; and identifying lifestyle factors that play a role in increasing cancer risk. Immunotherapy, which uses the patient's immune system to fight cancer, has changed treatment prospects for cancer patients globally.

In 2021, immunotherapy, in the form of anti-PD1 immune checkpoint inhibitor, was approved as a first-line treatment for advanced oesophageal cancer. We aim to have immunotherapy approved as a first-line treatment for all stages

of cancer. We do not yet know who will benefit most and how immunotherapies will interact with other treatments such as chemotherapy and radiotherapy, which can impact the immune system. The correct choice, dose and timing of treatment is crucial.

“Cancer is a complex disease driven by many underlying and external factors that can influence how a patient responds to treatment.”

Dr Joanne Lysaght

Associate Professor, Cancer Immunology and Immunotherapy Group, TTMI and Trinity St James's Cancer Institute

Dr Joanne Lysaght, Associate Professor, leads a multidisciplinary group at the Trinity Translational Medicine Institute

and Trinity St James's Cancer Institute. Dr Lysaght's group aims to identify new immunotherapies for oesophageal cancer patients, and investigate how and when to apply them alongside standard treatments. They also study how the tumour microenvironment affects immunotherapies. The Department of Surgery has established several tissue biobanks, which are key for this translational research. This research addresses key gaps in knowledge and will ultimately improve patient management, treatment choices and outcomes.



Pushing boundaries on Alzheimer's detection, prevention, cure and care

Alzheimer's disease (AD), the most common cause of dementia, occurs when toxic proteins accumulate in the brain, resulting in memory loss and impaired daily functioning. In the absence of definitive therapies for AD, clinical trials are essential for developing effective prevention, detection and treatment.

The Cognitive Clinical Trials Unit (CCTU) in Tallaght University Hospital (TUH) has become Ireland's leading AD clinical trials unit. Under Professor Seán Kennelly, the CCTU trials operate in parallel to the specialist clinical memory services at the TUH Institute of Memory and Cognition, offering patients access to novel interventions. An early adopter of routinely utilising cerebrospinal fluid AD biomarkers to support diagnosis in people with mild memory problems, this timely, accurate, biomarker-supported diagnosis facilitates clinical trials participation.

Better detection: The ENBIND study is longitudinally investigating potential immune and digital biomarkers indicative of cognitive

“We are at a very exciting tipping point in the quest to have our first definitive treatment for Alzheimer's disease”

Professor Seán Kennelly

Director of the Cognitive Clinical Trials Unit in Tallaght University Hospital

risk in otherwise healthy middle-aged people with Type 2 diabetes. Further projects with industry partners, such as the EI-funded GaitKeeper project, explore the use of artificial intelligence to analyse speech and walking pattern changes as digital biomarkers of cognitive decline.

Prevention: The BRAIN-Diabetes (Border

Region Area Lifestyle Intervention Study for Healthy Neurocognitive Ageing in Diabetes) project aims to develop a healthy brain lifestyle programme for people with Type 2 Diabetes Mellitus (T2DM) in the border areas of Ireland.

Cure: The EU201 study investigates a novel investigational medicine targeting toxic tau protein accumulations in the brain; while monitoring changes in neuroimaging, electroencephalogram and cognition, in people with mild AD.

Enhanced care: The VINCI-AD study is investigating the potential role for transcutaneous vagus nerve stimulation in promoting cognitive enhancement in AD.



The Irish childhood national diabetes register

Childhood Type 1 diabetes is potentially fatal. Poor disease control can cause life-limiting complications in childhood and adult life, including blindness, kidney failure and amputations. These are largely preventable through good metabolic (blood sugar) control. Diabetes control requires quality data to achieve more effective health service planning, resource allocation and targeted measures. Diabetes registers allow the monitoring of diabetes in populations. This helps us understand the condition and its causes. Until recently, Ireland had no such register.

In 2008 the Irish Childhood Diabetes National Register (ICDNR) was established to provide data on Type 1 diabetes in children and young people. Now in its 14th year, the ICDNR is unique internationally due to its scope and level of detail. It makes robust and accurate data available to support clinical care and audit. It provides anonymised data and prevalence forecasts to the Health

Service Executive (HSE) to inform its resource allocation and planning of services for diabetes care in children and young people. Its data also support targeted measures, quality clinical care, high-quality research and audit.

“Our monitoring has shown that we have an unacceptably high rate of life-threatening DKA at diagnosis that needs to be addressed.”

Professor Edna Roche

Consultant Paediatrician and Professor in Paediatrics

Research based on this register includes national monitoring of the incidence of diabetic ketoacidosis (DKA) at diagnosis. DKA is a serious and potentially fatal consequence of Type 1 diabetes associated with delayed diagnosis, which can increase the risk of complications in adulthood. The ICDNR

also leads a campaign in collaboration with Diabetes Ireland, supported by Novo Nordisk, to increase national awareness of childhood diabetes, promote early diagnosis and prevent DKA. The campaign materials were developed with students of the Technological University of Dublin at Tallaght.

Funded by the National Children's Hospital Foundation and hosted at Tallaght University Hospital, the ICDNR is led by principal investigator Professor Edna Roche and governed by a steering group with expertise in medicine, nursing, IT, statistics and health informatics.



SCHOOL OF MEDICINE RESEARCH STRATEGY 2021-2026

Research on ageing: From research to practice to policy

Falls are very common as people get older and many result in hospitalisations. Research led by Professor Rose Anne Kenny, Professor of Medical Gerontology and Director of the Mercer's Institute for Successful Ageing, showed that falls can be caused by underlying heart irregularities and exaggerated swings in brain blood flow. These abnormal blood pressure and heart rate patterns predict the adults at highest risk of future fractures as well as depression, cognitive impairment and mortality. This research, supported by subsequent policy changes, has significantly reduced the number of older people who are hospitalised after a fall.

The TILDA study showed that 25% of people aged 50-55 and 45% of people over 80 experience falls each year. Fifteen per cent require hospital care for injuries such as fractures and head injuries.

Using this information, fallers were assessed

in the emergency department (ED) using small implanted monitoring technologies which confirmed that heart irregularities were linked to falls. Resultant novel ED care

“The research reflects 15 years of work by multidisciplinary teams and illustrates how basic research and population studies can rapidly translate into clinical practice.”

Professor Rose Anne Kenny

Professor of Medical Gerontology and Director of the Mercer's Institute for Successful Ageing

pathways demonstrated a 50% reduction in hospital admissions and are being replicated globally. An annual syncope and falls clinical training program in Mercer's Institute for Successful Ageing at St James's Hospital, and a new module in Trinity College's Ageing

and Biogerontology Masters disseminates the research. The findings informed new recommendations in three recent international guidelines and an EU consensus paper.

The research is funded by national and international bodies, including the Health Research Board, Department of Health, Science Foundation Ireland, H2020, EIT, NIH/ NIA and philanthropy.



Exercise is key following a cancer diagnosis

The National Cancer Registry of Ireland reports an overall improvement in cancer survival. This means we have more cancer survivors, but many need physical and psychological help to improve their quality of life. Physical functioning is affected by the disease and side-effects of treatment (surgery, chemotherapy, radiation). Survivors may have low exercise tolerance, decreased muscle weakness and mass, and higher body fat. Restoring body composition and physical performance is needed to improve physical functioning and may also help prevent secondary disease, particularly cardiovascular, which is a risk for cancer survivors.

While we understand the benefits of exercise in preventing and treating cancer, we know less about prescribing individualised exercise programmes. Professor Juliette Hussey's research group in the Clinical Research Facility at St James's Hospital works on this topic with the Department of Surgery and Professor John Reynolds. Aiming to regain pre-diagnosis

activity level may not be enough, since about 65% of people in Ireland get too little exercise. Cancer survivors must make major changes in exercise levels to achieve health benefits.

“The expectation is that this research over the coming years will provide the evidence to support guidelines for rehabilitation including individualised exercise prescriptions.”

Professor Juliette Hussey

Professor in Physiotherapy, School of Medicine, and Vice President for Global Relations, Trinity College Dublin

Different cancers have different rehabilitation requirements. Complex diseases such as oesophageal cancer cause physical and nutritional impairment, and the usual treatments affect overall wellbeing. Findings from the ReStOre project (Rehabilitation

Strategies following Oesophageal Cancer), which includes prescribed exercise, show cardiorespiratory fitness can be improved without compromising body composition. This success formed the basis for ReStOre 2 (Rehabilitation Strategies in Oesophagogastric and Hepatopancreaticobiliary Cancer).

Prehabilitation (pre-surgery exercise training) would also help, but the time between diagnosis and surgery is often too short for typical exercise programmes to show benefits. However, high-intensity interval training can improve exercise tolerance within two weeks.



SCHOOL OF MEDICINE RESEARCH STRATEGY 2021-2026

A 'one-stop' health surveillance clinic for children with Down Syndrome

Down syndrome (or Trisomy 21) is the most common chromosomal abnormality, making up 8% of all such cases registered Europe-wide. In Ireland, one baby in 444 has Down syndrome: about 110 babies each year. Management of this condition has improved over the decades, thanks partly to healthcare programmes designed to improve life expectancy and quality of life for people with Down syndrome.

Researchers at Children's Health Ireland (CHI) at Tallaght University Hospital and Trinity College Dublin's Department of Paediatrics established a unique health-check clinic for children with Down syndrome. We realised that many services for Mid-Leinster patients were provided by non-statutory bodies. This is because, traditionally, care came from religious and charitable organisations dedicated to a single type of disability. This made access to, and coordination of, services variable and complicated.

We aimed high: for 100% of children with Down syndrome at CHI Tallaght to receive care in accordance with Irish and UK guidelines. We started twice-monthly 'one-

"Our project provides a framework which would be potentially emulated and used in other medical conditions."

Professor Eleanor Molloy

Professor of Paediatrics and Child Health

stop' multidisciplinary clinics catering for 270 children with Down syndrome. These clinics offered care by a clinical nurse specialist and same-day audiology and phlebotomy appointments. We found that compliance with guidelines improved with each clinic. Health promotion strategies, such as providing

information on immunisations, also became more effective. Parents reported 100% satisfaction, and we now plan to expand the clinic to include nutrition and dietetics, play therapy and interdisciplinary services such as cardiology, respiratory and mental health.

Nicola Hart from Down Syndrome Ireland explained: *"This and other research coming from the clinic is very welcome. It will help to inform best practice not just for those attending, but for children who have Down syndrome in other parts of Ireland and around the world."*



Cellular biomarkers of disease onset, progression and response to treatment for rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune disease which causes inflammation, pain, swelling and stiffness in the joints. This can rapidly damage cartilage and bone, leading to significant joint destruction and functional disability. Currently we cannot predict who will develop severe, erosive disease, or who will respond to treatment. As the treatments are very expensive, 'trial and error' is not cost effective. Introduced early, biological therapies consistently produce better long-term outcomes, limiting joint damage and disability and allowing employment. Our research focuses on people with, or at risk of, RA. We seek to understand the evolution of RA and identify cellular/soluble biomarkers to predict disease onset and potential new targets for therapy.

Identifying those at risk of developing RA remains problematic. Not all the individuals whose blood contains autoantibodies (ACPA)

go on to develop RA, and we have not yet identified blood or cellular biomarkers that can accurately predict it. RA patients and at-risk individuals with ACPA have taken part

“This research will lead to a better understanding of disease onset and progression.”

Professor Ursula Fearon

*Professor of Molecular Rheumatology
Trinity College Dublin*

in a study of blood monocytes as potential biomarkers under Professor Ursula Fearon at Trinity Biomedical Sciences Institute with the Centre for Arthritis and Rheumatic Diseases at St Vincent's University Hospital (www.rheumatologytcd.com). Monocytes are involved in joint inflammation, and detecting

them early may indicate that RA symptoms are likely to set in.

We studied the hyper-inflammatory and hyper-metabolic nature of these monocytes, and showed how they migrate to the joints and set off further inflammation there. Identifying these cells at a pre-disease stage may therefore help us predict the onset of RA and start treatment early (which saves both cost and suffering), and also suggest new lines of treatment through metabolic reprogramming of cells.



SCHOOL OF MEDICINE RESEARCH STRATEGY 2021-2026

A new method of measuring satiety in clinical trials of hyperphagia and obesity

Prader-Willi Syndrome (PWS) is associated with impaired satiety control: not knowing when you have had enough to eat. Symptoms include hyperphagia (over-eating) and extreme obesity. Caregivers of people with PWS need constant vigilance around food, as uncontrolled or unsupervised eating may result in gastric rupture and death. The development of effective hyperphagia treatments is a priority for the PWS community.

We are currently testing new drugs for obesity that could be life-changing for people with PWS. However, we currently have no objective way of measuring hyperphagia, which makes it difficult to chart improvements during clinical trials. Measures such as the Hyperphagia Questionnaire or BMI are limited as they rely on environmental control measures, such as food security. Our study aimed to develop a novel biomarker of satiety by using eye-tracking and food-related attentional bias (FAB). Drawing

on skills and knowledge from neuroscience, endocrinology, psychiatry and psychology, we designed a FAB task as a biomarker. It involves tracking people's eye movements as they look

“Developing a biomarker of satiety for clinical trials of hyperphagia is a challenging task and requires expertise, skills and resources from multiple disciplines and stakeholders.”

Sarah-Marie Feighan

PhD student supported by the School of Medicine Studentship Award and the Sarah Purser Medical Research Award

at food stimuli. The FAB task can apply at all stages of development and different levels of

cognitive ability. We used it to show that adults look longer at food stimuli when hungry (after a four-hour fast) than when satiated (30 minutes after eating).

Our next step is to validate the FAB task in children and adults with PWS. If successful, it will be the first objective biomarker of satiety that could be used to monitor the effectiveness of medicines for hyperphagia in PWS. The FAB task may also be used as a stratification marker to compare behavioural characteristics in clinical trials of obesity.



Pioneering international research into transforming health systems

Catastrophic events over the last decade or so have highlighted the challenge of governing health systems at times of shock. The rapid spread of COVID-19 has severely tested almost all the world's health systems. From 2008, economic austerity affected many high-income countries. Health system resilience is important to help us cope with current and future shocks and improve performance. The RESTORE programme, a five-year Research Leader Award funded by the Health Research Board, investigates how best to enhance health system resilience, achieve reform and improve staff wellbeing in Ireland and internationally.

RESTORE (Towards Dynamic Resilience in Health System Performance and Reform) evaluates the strategies and metrics used to monitor and build health system resilience internationally, and assesses the resilience of the Irish health system before, during and after the COVID-19 pandemic. It reviews international experience of managing complex

whole-system reforms such as Sláintecare, and investigates how shocks such as COVID-19 and the 2008 financial crisis challenge or even facilitate reform. A key focus will be how such

“Shocks create opportunities for innovation and long-lasting health system reform. Now is the time to invest in our health systems for better performance.”

Professor Steve Thomas
Edward Kennedy Chair for Health Policy and Reform

shocks affect the Sláintecare programme, and how to ensure its full implementation despite the difficulties. Resilience and reform depend on support from staff, and RESTORE will also focus on HSE staff wellbeing and motivation as both a sign of resilience and a precondition for change.

RESTORE is headed by Professor Steve Thomas, the Edward Kennedy Chair for Health Policy and Management. His team of Irish and international researchers, influencers and policy-makers aims to evaluate and strengthen health system resilience and to share the understanding they gain with policy-makers in governments and agencies such as WHO, OECD and the EU. It will develop evidence-based strategies to enable policy-makers to balance performance against reform and achieve universal care by improving resilience.



SCHOOL OF MEDICINE RESEARCH STRATEGY 2021-2026

Better ways to tell our story

At the heart of this research strategy 2021-2026 is a passion to better tell our story so that the School of Medicine and its outstanding research teams will gain the recognition and support they deserve.

As research impact officer in the School of Medicine, I am privileged to outline an exciting variety of processes, systems and training which shape and showcase the diversity and excellence of our researchers' activities. Chief among these initiatives is the successful lunchtime seminar series: Early Career Researcher Training for Impact. Designed for our early- and mid-career health researchers, the seminars share best practice in career development and how to build research profiles and frame proposals for maximum impact.

The appointment of a Science Communications Officer helps us celebrate the achievements of our researchers and inform the world of our

research impact. In consequence, we have seen an unprecedented increase in traffic to our website and social media channels.

“A broader understanding of the societal impact of research has a particular resonance with the School of Medicine.”

Bridget Gavin

*Research Impact Officer, School of Medicine
Trinity College Dublin*

Although the main impact is to convey a broader understanding of the social, cultural, environmental and economic benefits of research, the School's performance in terms of conventional metrics (e.g. citations, number of papers) remains the bedrock of our QS World University Rankings and Times Higher Education World University Rankings.

To offer an authoritative assessment of our research productivity, we have produced a research impact analysis that explores, defines and summarises our output over the 2015-2020 period. This tool for management intelligence shows the School's research performance and trends in a national and global context.

By defining better ways to identify, measure and communicate our research impact, we will establish a robust context in which to frame the School's research strategy for the next decade and beyond.



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