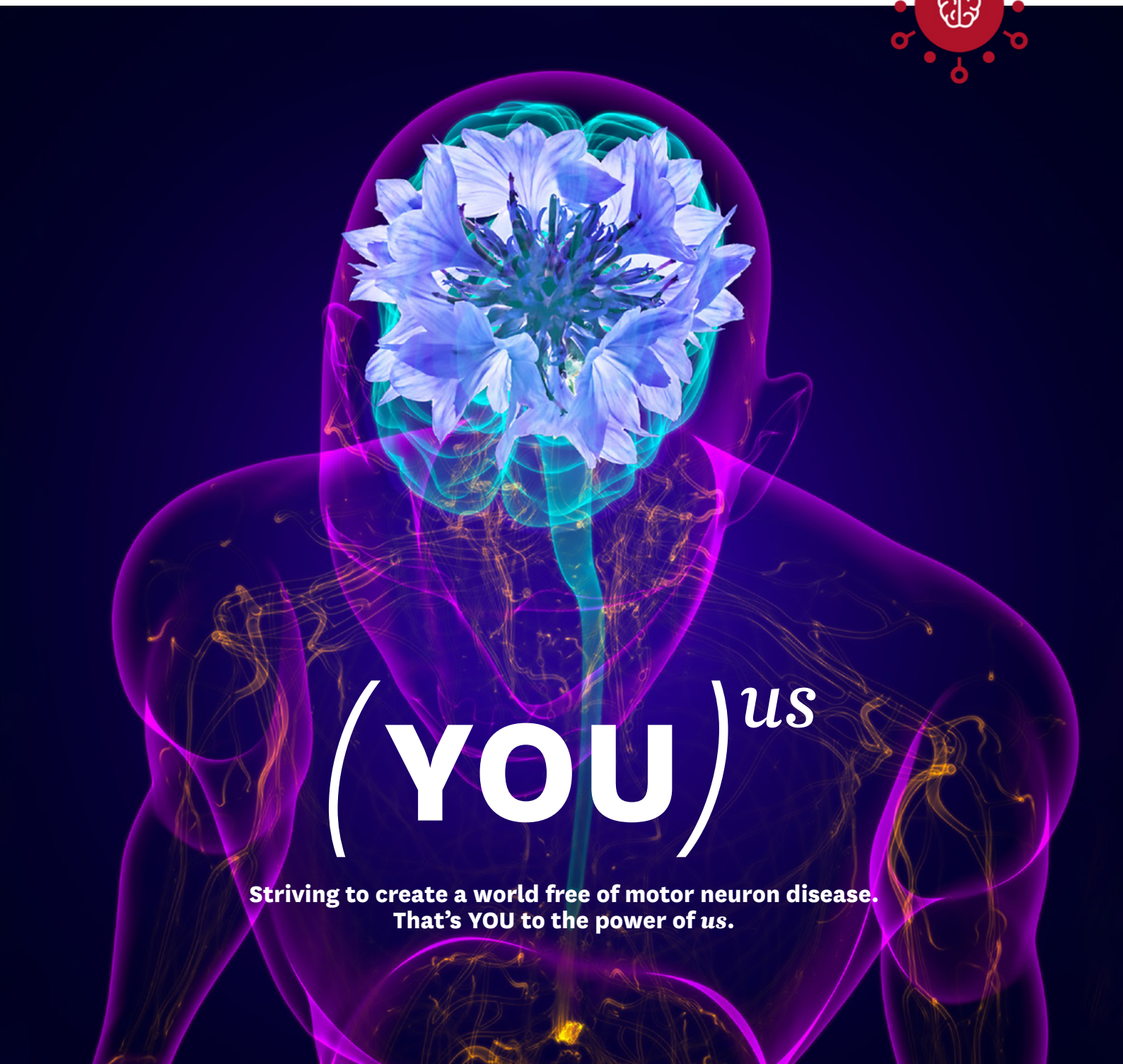
FACULTY OF MEDICINE, HEALTH AND HUMAN SCIENCES

MACQUARIE University
SYDNEY·AUSTRALIA

Macquarie University Motor Neuron Disease Research Centre 2023



Foreword

The Centre for Motor Neuron Disease Research exemplifies Macquarie University's commitment to doing quality research with real-world impact. The Centre's research in motor neuron disease (MND) and related neurodegenerative diseases is outstanding.

Professor Patrick McNeil

Deputy Vice-Chancellor
(Medicine and Health)

Managing Director | MQ Health

Executive Dean | Faculty of Medicine,
Health and Human Sciences

Professor Sakkie Pretorius

Deputy Vice-Chancellor (Research)

It again gives us great pleasure to contribute this foreword for the Macquarie University Motor Neuron Disease Research Centre biannual report.

The Centre has continued to develop and grow to become home to Australia's largest clinical and research program in MND. In their mission to provide world-class care for people living with MND and to develop new effective treatments for this devastating disease, the Centre is an exemplar of the University's aim to perform high-quality research with real-world impact.

Since the previous report, the Centre has continued to make seminal contributions to understanding the molecular and cellular basis of MND. Importantly, the Centre is increasingly translating their discoveries to preclinical and clinical research. Macquarie University has become widely known for MND research and clinical care thanks to the hard work and dedication of this team of researchers, clinician-scientists and research students.

The Centre is a flagship of MQ Health, the University's academic health science centre. This Centre exemplifies the MQ Health model as an integrated health sciences centre, with collaborative research between the clinic and the laboratory. In common with the academic health science centres that exist overseas, MQ Health's vision is to integrate research and teaching with clinical services to deliver the highest quality healthcare to its patients. As evidence of their commitment and evolving vision to improve the lives of MND patients, the Centre hosted six clinical trials of potential MND therapies in the past two years, including large multi-centre international trials as well as the first Macquarie sponsored and led clinical trial.

The Centre builds on the intensely personal care delivered to MND patients by Professor Dominic Rowe and his team in MQ Health Neurology. The clinical MND research is led by Rowe, including clinical trials and the nationally unique Macquarie Neurodegenerative Diseases Biobank that provides resources to enable the cutting-edge research of the wider team and their collaborators. By linking Professor Rowe's clinic and research with that of fundamental research, preclinical and translational research, the Centre has created a discovery and therapeutic development pipeline that is internationally leading. Indeed, their Macquarie-led spin out company (Celosia Therapeutics) seeks to develop candidate MND gene therapies based on the Centre's research outcomes.

We commend to you the research achievements outlined in this report and especially the Centre's vision for the next stages of research and translation as they strive for a world without MND.

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Introduction

As we mark 10 years since Macquarie University launched the motor neuron disease (MND) research program, we acknowledge the successful research outcomes and embrace the challenges that lie ahead for the MND Research Centre as it continues to strive to better understand, diagnose and treat MND.

In 2013, multiple researchers sharing a dream to beat MND came together from five institutes across Australia. With complementary expertise, they progressively built a research centre at Macquarie University. Central to this goal was integrating multiple scientific disciplines in a co-ordinated research 'pipeline' that engages patients in research.

This enterprise came to be known as the MND Research Centre. The Centre links the Multidisciplinary MND Service and Clinic as part of MQ Health Neurology with Australia's largest MND patient biobank and the research laboratories. Working together, the Centre, the Clinic and the Biobank facilitate our breakthrough discoveries to better understand MND, accelerate new drug discovery and evaluate therapies in clinical trials.

Our strategy has sustained growth in MND research and catalysed new major national and international collaborations. We continue to attract and develop exceptionally talented, dedicated researchers who work closely with the Clinic and are driven by the desperate need to beat MND.

Integral to the operation of the Centre is the care of people who have MND. We provide integrated care to more than 200 people with this disease, from initial diagnosis to multidisciplinary management of a complex and changing disease, to care in the community and end-of-life care. MND affects every person distinctly, and in much the same way, their families are also affected very differently.

The whole focus of our research effort is to change the survival and quality of life of people with MND. We use a patient-centric model of care to achieve the best outcome for people with MND. Until we can stop the progression, MND will continue to cause the death of more than 800 Australians each year.

Our role and progress in research and clinical care represent a team effort. From a standing start in 2013, we are now the largest MND research facility in Australia, and one of the largest MND research centres in the world, with multiple strands of funding from government and not- for-profit sources. Thank you to all of those involved in bringing this report together. We look forward to sharing with you the progress in the battle to slow and stop this devastating disease. Also, a special thank you to all of our generous donors who continue to enable us to strive to better understand, diagnose and treat MND.

Professor Julie Atkin

Centre Co-Director and Group Leader

Professor Ian Blair

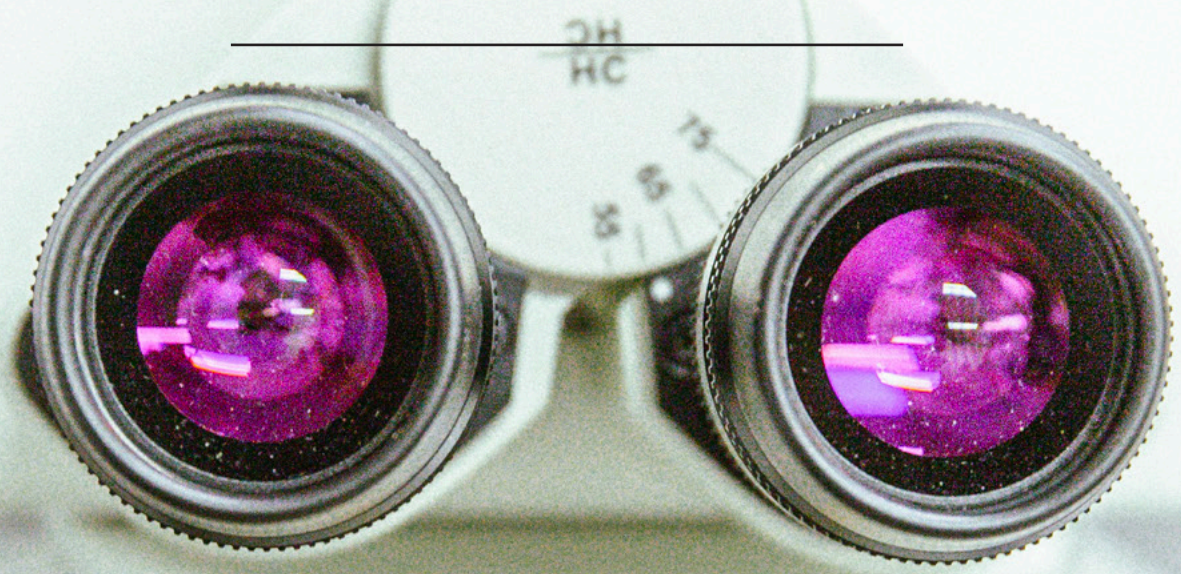
Centre Co-Director and Group Leader

Professor Dominic Rowe AM

Centre Deputy Director

Our vision

is a world without MND.



Our mission

is to provide world-class care for people living with MND and to develop new effective treatments for this devastating disease.

Achievements 2022/2023

One of the world's strongest multidisciplinary hubs researching MND.

Produced > 100 original research publications in international peer-reviewed journals.

Set up Australia's first indigent fund for MND patients unable to access care.

Australia's largest longitudinal MND biobank.

Received > $6.0 m of grants and fellowships.

Home to more than 90 researchers working on MND.

Provided comprehensive care for 10% of Australians living with MND.

Several clinical trials including:
3K3A-APC, CuATSM, Lighthouse 2, Atlas and Wave

>500

Working with more than 500 global research partners.

Genetic testing results in babies born through IVF without a faulty MND gene.

Received >$3.5m

in philanthropic funding.

Launched and hosts the annual Macquarie Neurodegeneration Meeting.

Global studies to identify genes associated with MND.

Developing the next generation of leaders in MND research.

5

Applied for 5 patents based on research outcomes from the Centre. Established a spin out company that seeks to develop MND gene therapies based on the Center's research discoveries.

Postgraduate student training program in MND research.

Showcasing ten years of impactful research

Ten years ago, five research groups came together who shared a dream to conquer motor neuron disease.

Combining their complementary expertise from institutes across Australia, the team progressively built a coordinated clinical and research enterprise that came to be known as the Macquarie University MND Research Centre. Today it is the largest MND research centre in Australia, employing more than 90 people and that dream is much closer to becoming reality.

"Ten years ago I could not even have imagined that we would be working on a possible cure," says Professor Roger Chung. "But today we are."

Centre members are part of Macquarie University's Celosia Therapeutics, a new company Neurochemistry and Molecular Therapeutics that is backing their research and accelerating their quest to start clinical trials as soon as possible.

TRANSLATIONAL RESEARCH

The Centre works closely with the Multidisciplinary MND Service and Clinic. The clinic is led by Professor Dominic Rowe, an expert in neurodegenerative disease and the inaugural Professor of Neurology at Macquarie University, Rowe started the clinic when Macquarie University Hospital opened in 2010 and it was one of Australia's first. Today it is Australia's largest MND clinic.

"This relationship with the clinic means that we are a translational research centre - we don't just research in isolation but our research is used to develop new ways to diagnose and treat MND. Patients from the clinic can take part in international clinical trials. This means we have an impact on people's lives," says Professor Ian Blair, one of the Centre's co-directors.

The MND Research Centre also established the Neurodegenerative Disease Biobank which is now one of the largest in the world. During regular clinic visits, MND patients and family members donate blood, skin, urine and hair samples.

The biobank staff store these samples and the researchers can also access them using strict protocols. This means researchers analyse how the disease progresses over time, as well as investigate causes and therapies. Dr Sarah Furlong leads the biobank.

In the last decade, the Centre has become more interdisciplinary and expanded from the original five to eight interconnected research teams. "We foster emerging researchers and some have gone on to lead their own teams within the centre," Blair says.

PUBLICATIONS AND TRIALS

Since it was created, the Centre has produced more than 400 peer-reviewed journal articles. These publications reported the Centre's breakthrough discoveries to understand the causes of MND, how it progresses, and the mechanisms that can be targeted by potential therapies. The Centre also has multiple new potential drugs in development that have shown efficacy in mouse, zebrafish and cellular disease models. It also commenced multiple clinical trials, directed by Rowe, in the past two years.

These include the ATLAS trial of Tofersen, a gene therapy for patients who carry a mutation in the SOD1 gene as the cause of MND. The Centre also completed a clinical trial for 3K3A-APC in MND, a possible therapy that has both anti-inflammatory and neuro-protective effects. Other patients with sporadic MND are participating in the Lighthouse 2 Trial, an international Phase 3 clinical trial that's repurposing an antiretroviral therapy.

The Centre continued to host the annual Macquarie Neurodegeneration Meeting, a national conference attended by leading national and international speakers and more than 200 delegates.

Left to Right: Dr Sarah Furlong, Professor Julie Atkin, Professor Roger Chung, Associate Professor Marco Morsch, Professor Ian Blair, Associate Professor Kelly Williams, Associate Professor Angela Laird, Professor Dominic Rowe, Dr Albert Lee.

Our research teams

'Success would look like us being able to slow and stop this disease that's robbing families of fathers, mothers, wives and husbands, sons and daughters ... If we can stop some deaths, that's success.'

- Professor Dominic Rowe

NEURODEGENERATIVE
DISEASE BIOBANK

Biobank critical for future research

The MND Research Centre's Neurodegenerative Disease Biobank is a world-leading resource.

Established a decade ago, the biobank at the MND Research Centre holds more than 60,000 biological samples of nine different sample types extracted from blood, urine, hair, spinal fluid or skin from 1,100 people. It's now one of the largest of its kind in the world.

Over the last decade, the value of the biobank has grown exponentially, says Dr Sarah Furlong who runs the facility. "We have a large collection of biological samples linked to extensive data collected longitudinally from patients, family members and controls. This puts the biobank in a position to be capable of supporting large diverse research projects."

Patients attending the Multidisciplinary MND Service and Clinic along with their family members and supporters are invited to donate samples to the Biobank to enable comparison between those with MND and those without. These samples are an invaluable resource for researchers to increase understanding of MND, and to identify treatments and preventative measures.

Sample types collected include include blood (to extract plasma, serum, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), peripheral blood mononuclear cells (PBMCs)), urine, hair, cerebrospinal fluid (CSF) and skin (to isolate fibroblasts).

The Biobank also collects extensive demographic, lifestyle and clinical data, which is uploaded to a dedicated database. This increases the power of the research immensely.

BOOSTING RESEARCH

In the last decade, researchers have used over 4,500 biobank samples in more than 30 research projects - nine in the last year alone - across the fields of genetics, proteomics, cellular stress, biomarkers and environmental studies. These projects include collaborators across Macquarie University, nationally and overseas.

Several projects take advantage of the longitudinal collections of samples linked with extensive clinical data to identify disease biomarkers. "Discovery of sensitive and specific biomarkers is helping clinicians with diagnosis, improving patient outcomes, improving the design of clinical trials and helping to develop novel therapeutics," says Furlong.

The Biobank is part of an Australian consortium called the Sporadic ALS Australia Systems Genomics Consortium—SALSA-SGC. This consortium comprises nine MND centres across Australia working together to build an integrated infrastructure. Their focus is to ensure the centres follow global best practice standards in their data collection and storage.

The Biobank is also a member of a global collaboration, Project MinE, which aims to analyse the DNA of more than 15,000 MND patients and 7,500 control subjects from 20 countries. The aim of Project MinE is to identify what causes sporadic MND. They also collaborate with other researchers globally on different projects.

SAFETY FIRST

The Biobank follows a number of measures to ensure the samples are safe in an emergency," says Furlong, who is also the Clinical Research Manager at Macquarie's Faculty of Medicine, Health and Human Sciences. "We divide every collection into two separate freezers in different locations, with temperature alarms linked to staff phones and ensuring the freezers are backed-up by generators."

A robotic instrument called a QIASymphony extracts DNA from blood rapidly and consistently. Other high-tech instruments measure sample quality. Ultra-low temperature freezers maintain sample integrity by freezing the samples at as low as –196°C. Samples and data are coded to protect the privacy of the participants.

In the last year, David Poynter, the biobank's system's developer has created a bespoke sample tracking system within the biobank database, tailored to the very specific requirements of its users.. This system makes it possible to keep an inventory of the 60,000 samples throughout their lifecycle: from collection to processing to storage and ultimately use in research.

"We're moving away from a manual way of tracking samples to a new system that really streamlines the operation of the Biobank and makes our work more effective and higher quality," Furlong says.

NEURODEGENERATIVE DISEASE BIOBANK TEAM

Manager
Sarah Furlong*

Systems Developer
David Poynter*

Biobank Co-ordinator
Susan D'Silva*

Biobank Technician
Elisa Cachia*

Biobank Technician
Oluwaseun (Samuel) Ishola*

**Pictured*

The collections are processed into nine different sample types: plasma, serum, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), peripheral blood mononuclear cells (PBMCs), urine, hair, fibroblasts and cerebrospinal fluid.

GENETICS AND
GENOMICS TEAM

Gene research leads to family clues

Mapping MND patients' genomes leads researchers to identify inherited genes and develop targeted treatments.

Identifying the genes that cause or increase the risk of developing MND is the focus of the Genetics and Genome team, which is working with an international consortium of researchers. Led by Professor Ian Blair, the team analyses DNA gathered from patient samples kept in the neurodegenerative disease biobank.

Blair and his colleagues map MND patients' entire three billion letter genetic code to spot the genes that cause or confer risk of MND. So far, more than 20 familial MND genes have been identified by researchers around the world.

ONE OF THE FIRST INHERITED GENES

Blair was part of the Australian and British research group in 2006 that discovered mutations in TDP-43. They found that the mutant gene TDP-43 became toxic and caused MND in a percentage of patients. This confirmed that abnormal TDP-43 protein, which is seen in almost all patients, is central to the pathology of MND.

"I was very excited to be part of that discovery and we received a lot of international media coverage," he says. "The discovery triggered a boom in MND research globally. Until then, we had known very little about the disease biology."

Sixteen years later, Blair and his team at the Centre for MND Research are still building on that initial discovery and have made many others. Greatly enhanced genome mapping techniques and collaboration with coding experts who use high-powered computers accelerates their research.

"It's a huge breakthrough to be able to map the MND patient's entire genome which allows us to contrast them with people who don't have MND," Blair says.

The cost of genome mapping has dropped dramatically from about $50,000 per person to about $1,000. It can also be done a lot faster, which makes it a lot more cost-effective for research purposes.

That can lead to more rapid diagnosis of the disease and mean patients can take part in clinical trials quicker as well. Inherited gene mutations cause about 10 per cent of MND cases.

In 2016, Blair and Dr Kelly Williams published another important discovery of mutations in CCNF gene (which encodes cyclin F protein) in MND patients. This discovery was one of the main premises for Professor Roger Chung to set up his Neurochemistry and Molecular Therapeutics Team within the Centre. Then in 2019, Williams launched her own team.

GENETICS AND GENOMICS TEAM

Group Leader
Professor Ian Blair*

Postdoctoral Research Fellow, Team Leader
Dr Shu Yang*

Postdoctoral Research Fellow
Dr Sandrine Chan*
Dr Jennifer Fifita*
Dr Alison Hogan*
Dr Emily McCann

PhD Student
Natalie Grima*
Sharlynn Wu*

Research Assistant
Amy Ding*

**Pictured*

GENE KNOWLEDGE

The Genetics and Genome team also looks at the MND patient's age when symptoms first appear and how the disease progresses. "If we can identify which genetic or genomic factors make the motor neurone die, we can work to design therapies to delay progression of the disease and maximise the length and quality of life for MND patients," Blair says.

The genetic information Blair's team identifies is channelled back into the Multidisciplinary MND Service and Clinic to inform the genetic counsellors who work with MND patients and their families. Finding a hereditary genetic cause for MND can have an enormous impact on individuals and families, he says.

"When families find out they have MND, it means they may have up to 50 per cent of any one generation developing the disease; perhaps a brother, sister, aunt, uncle or parent died from the disease, and before that, a grandparent. So MND is very much in the forefront of their lives," Blair says.

MND patients with familial MND can undergo genetic diagnostic tests. Researchers can identify a known mutation in about two thirds of these families. "If these family members want to have children, genetic testing and IVF technology offers the opportunity for some to see these faulty genes stop at their generation," Blair says.

Simultaneously, the team is also in the process of identifying gene variations that put people at risk of developing sporadic MND, whether it is triggered with lifestyle choices or exposure to environmental factors, by cataloguing the variations.

GENOMICS AND
BIOINFORMATICS TEAM

Mapping MND's genetic links around the world

How are MND families related? Macquarie researchers use computational analysis to discover 'cryptic relatedness' amongst MND patients worldwide.

Associate Professor Kelly Williams has long been fascinated by the genetic links between MND patients, their extended families and more distant relatives around the world. How exactly they are genetically linked is one of the big questions her Genomics and Bioinformatics team are exploring. A more detailed picture of disease will emerge by uncovering gene defects leading to MND.

Their first step is to examine DNA samples from MND patients. Using algorithms developed by team member Dr Lyndal Henden, they find shared regions of the human genome that have come from a common ancestor, revealing a shared 'cryptic relatedness'. They then search within these ancestral regions of the human genome to pinpoint the specific genetic defect in the DNA sequence causing MND.

"Our new methodologies allow us to perform more powerful genetic studies of MND patients , which is very exciting," says Williams. "When we are searching for a genetic defect that causes MND, the power comes from having more than one person to directly compare their genomes."

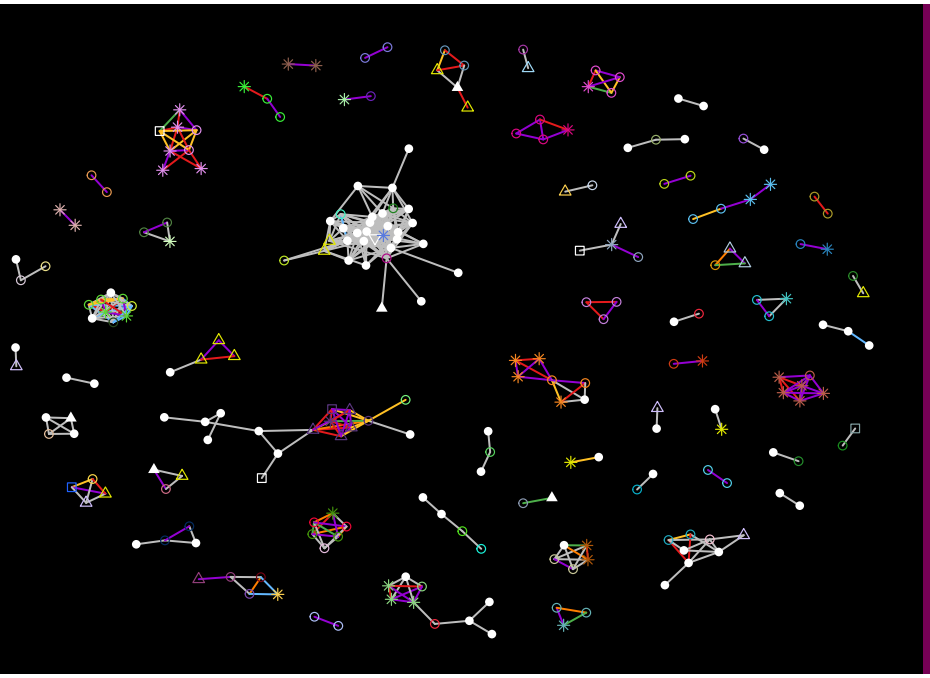
Bioinformatician Dr Dean Southwood looks at the genetic modifiers of the disease that might not actually cause MND but could influence when MND develops and how rapidly it progresses. These biological modifiers may be present in either DNA or Ribonucleic acid (RNA).

"If we can get a snapshot of the gene products that are active in the RNA at any time, then we can compare those in large cohorts of individuals with MND," says Williams.

In 2022, Williams and Henden received funding from the National Health and Medical Research Council to expand their MND genome dataset from MND patients in Australia to include more than 10,000 international MND patients from New Zealand, United Kingdom, Europe and North America.

They are collaborating with the University of Auckland, King's College London and Project MinE, a global MND genome sequencing consortium comprising 20 countries. The funding supported recruitment of Andrew Smith, a specialist Clinical Bioinformatician who is developing a computational framework to trawl through hundreds of terabytes of genomics data.

"In Australia, we still have more than 100 MND families without a known genetic defect, often because MND is a late onset disease and we don't have DNA from other relatives," says Williams. "Hopefully our cryptic relatedness work will lead to answers for these families."



CLUES IN BRAIN TISSUE

Team member, Natalie Grima, who is a PhD student, is taking a lab-based approach. She's comparing patient samples from the Neurodegenerative Diseases Biobank collected during patients' disease progression with brain tissue collected after their death. By comparing control participants with patients with early onset MND and patients with late onset or very rapid disease progression, she's hoping to find biological clues of the variability in disease.

"Natalie is obtaining DNA and RNA samples from brain tissue to see whether, by looking at the actual affected disease tissue, she can find more disease-relevant answers — maybe gene defects that are only present in the brain," says Williams.

GENOMICS AND BIOINFORMATICS TEAM

A GENETIC BASE

Williams completed her PhD with Professor Ian Blair at the University of Sydney. Then, after she received the competitive MNDRA Bill Gole MND Postdoctoral Fellowship, Blair recruited her to be part of his team at the nascent MND Research Centre at Macquarie University. She was one of the founding members and helped establish the Neurodegenerative Disease Biobank.

In her years at the Centre, Williams has played a central role in critical breakthroughs as part of the team that identified causal mutations in several genes. Her research has directly translated into clinical practice with these disease genes now added to diagnostic tests worldwide, including preimplantation genetic diagnosis (PGD) and pre-symptomatic testing.

In 2020, she was promoted to Head of the Genomics and Bioinformatics team. She's now Co-Director of Research at Macquarie Medical School.

Group Leader
Associate Professor Kelly Williams*

Postdoctoral Research Fellow
Dr Lyndal Henden*
Dr Dean Southwood*

Clinical Bioinformatician
Andrew Smith*

PhD Candidate
Natalie Grima*

**Pictured*

NEUROINFLAMMATION
AND NEUROTOXICITY TEAM

Hunt for biomarkers and environmental triggers

Searching for biological markers to determine the rate of progression and severity of MND, and identifying possible environmental triggers, are the two main areas of focus for Professor Gilles Guillemin's team.

Professor Gilles Guillemin oversaw the study that identified the world's first biological markers, or biomarkers, for suicide in 2013, Multiple Sclerosis in 2017, for breast cancers in 2020, for Alzheimer's disease and for dengue fever in 2022.

His research on neuroinflammation, neurotoxicity and the amino acid tryptophan is renowned internationally. Neuroinflammation is inflammation of the nervous system, including the brain and spinal cord. Neurotoxicity is when the nervous system is exposed to natural or manufactured toxic substances that alter its normal activity and/or kill nerves or brain cells.

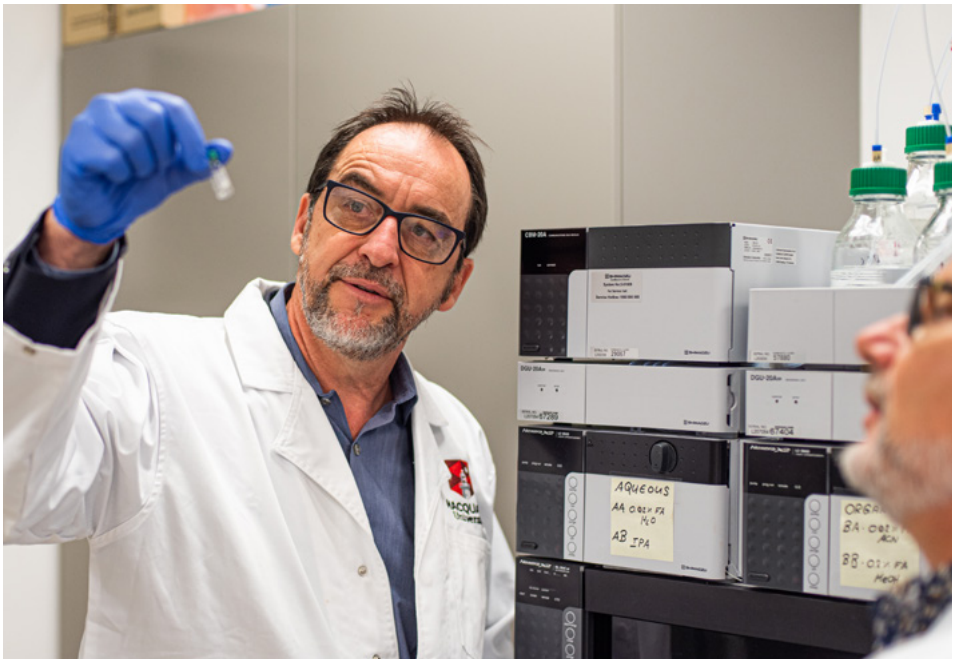
BIOMARKERS

With Professor Dominic Rowe, Guillemin co-created the Neurodegenerative Disease Biobank, the largest facility of its type in Australasia. His team analyses blood stored in the Biobank that is collected every six months from MND patients and their relatives (as controls) who attend the Multidisciplinary MND Clinic.

The team's aim is to identify new blood biomarkers able to predict how fast the disease is progressing — and whether patients respond to treatments or not.

ENVIRONMENTAL FACTORS

The team is also investigating possible environmental triggers that may lead some people to develop MND. Using data collected by MND Australia and the Multidisciplinary MND Clinic, Rowe has identified 'hotspots' in NSW, where the incidence of the disease is up to five times higher than the average. One such hotspot is the town of Griffith in the Riverina of central New South Wales. The team is studying urine samples from about 30 people with MND living in the region and is actively seeking new participants for the study.



"Because Griffith is an agricultural area, we are checking for more than 50 different pesticides, for 10 metals such as iron, copper, mercury and arsenic—and for cyanotoxins—to find out why these people are developing MND more than the rest of the population," Guillemin says.

In collaboration with the University of Orleans in France, his team recently showed the offspring from pregnant mice exposed to inflammatory stimuli followed by exposure to BMAA and herbicides glyphosate and glufosinate have long-lasting motor alterations; that could be consider as "MND-like symptoms".

MICROORGANISMS

Dr Benjamin Heng, in collaboration with the University of Sydney, initiated a new research project looking at the possible roles of microorganisms (viruses, bacteria and fungi) as another potential environmental cause of sporadic MND.

NEUROINFLAMMATION AND NEUROTOXICITY TEAM

CYANOTOXINS AND MND

Cyanotoxins are created by cyanobacteria, commonly called blue-green algae, which bloom at warm temperatures in stagnant or slow-running water that contains high levels of nutrients, such as runoff from farmland.

With other research teams based in the US, France, South Africa and Australia, the team is assessing whether beta-Methylamino-L-alanine (BMAA) and other cyanotoxins may trigger MND.

"The number of people dying from MND has doubled over the past two decades and this has interestingly paralleled the number of algal blooms in NSW in this period," Guillemin says. Dr Benjamin Heng and M. Hamed Panahi have looked at how BMAA damages DNA in cells and the role of a new neurotoxic pathway induced by BMAA called ferroptosis.

Group Leader
Professor Gilles Guillemin*

Lecturer
Dr David Lovejoy*

Research Fellow
Dr Charlie Ahn*
Dr Benjamin Heng*

Research Officer
Dr Sharron Chow*

PhD Student
Mona Dehhaghi*
Bahar Kavyani*
Seyed Hamed Kazemi Shariat Panahi*
Ananda Staates Pires*
Asma Oummadi*
Mahsa Vaez Zadeh*
Shivani Krishnamurthy*

** Pictured*

Neurotoxicity is when the nervous system is exposed to natural or manufactured toxic substances that alter its normal activity and/or kill brain cells.

NEURODEGENERATION
TREATMENT TEAM

Testing treatments: fish to rodents

Deepening research and expanding testing to natural compounds in the search for a treatment for MND.

Researchers within the Neurodegeneration Treatment Team are testing potential treatments on zebrafish and rodent models. These studies help the team better understand the degeneration of the nervous system that occurs in people with MND and discover the most effective treatments.

"The big difference in the last year is that we've started taking what we call 'hits', which are treatments that we have found to be protective within our zebrafish studies, and then started investigating them in greater detail, including using rodent models." Says Associate Professor Angela Laird, who leads the team.

REACHING THE BRAIN

Laird's team is now conducting short-term targeted testing on rodent models to ensure the treatment can reach the brains before expanding into longer studies.

One way is to implant fibre optic microscopes into the rodent models to watch whether the treatment is affecting levels of a fluorescent marker. "With this marker, we can actually see in the live, conscious animal whether a treatment is hitting its target, in real time, and identify if we need to increase the dose or change the administration route of the treatment," she says.

The researchers initially conduct a short term study to determine the dose and the best way to administer the drug. Then they undertake a longer 'efficacy study' of the therapy, when they observe whether it prevents the animals from developing neurodegeneration or movement deficits.

"This ensures that a treatment we examine in the lab has the best chance of making it into the clinic," Laird says. Her team is currently testing treatments on rodent models that they'd previously tested on zebrafish, such as those published back in 2017.

BEGINNING WITH MJD

Prior to joining the MND Research Centre in 2016, Laird used zebrafish to study neurodegenerative diseases with a leading MND team at KU Leuven, Belgium. She then established her own team at the University of Sydney's ANZAC Research Institute and led a project that produced and characterised the world's first zebrafish model of spinocerebellar ataxia type-3 (also known as Machado Joseph disease, MJD).

MJD is a fatal genetic neurodegenerative disease that develops in a similar way to MND, causing difficulties with movement and rendering patients immobile and dependent on their carers. Today, Laird's team investigates treatments for MJD and MND and she feels that these investigations complement each other.

NEURODEGENERATION TREATMENT TEAM

Group Leader
Associate Professor Angela Laird*

Lecturer
Dr Emily Don

Postdoctoral Research Fellow
Dr Maxinne Watchon
Dr Ignacio Simo

Research Assistant
Kristy Yuan
Julia Kam*
Andrea Kuriakose*
Sunny An*
Esmeralda Paric*

PhD Student
Katherine Robinson*
Prapti Chakraborty

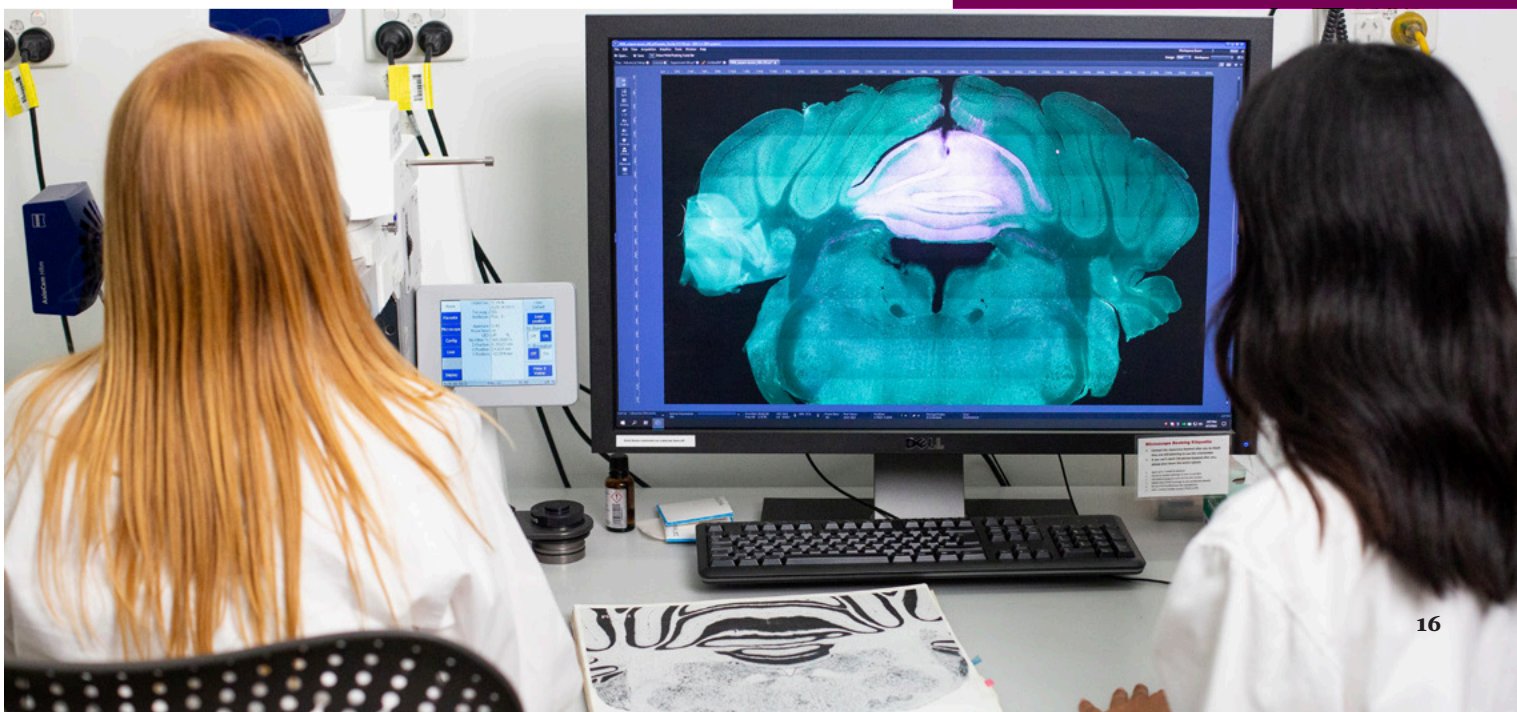
Masters Student
Vasilisa Zvyagina*
Brooke Bonnell*
Anastasiya Potapenko*

** Pictured*

DRUGS AND NATURAL COMPOUNDS

Within one study funded by the National Health and Medical Research Council, Laird's team is in the midst of testing natural compounds produced from plants and marine invertebrates. This involves collaborating with the Griffith Institute for Drug Discovery at Griffith University. Within this study the team are testing a library of natural compounds for those with protective effects on zebrafish models of disease. This testing is nearly complete and they will soon start testing the identified hit treatments further in the zebrafish, cultured cells and rodents.

In related projects, Laird's team is also collaborating with Professor Julie Atkin's Cellular Neurobiology team to explore other potential drugs on zebrafish affected by MND, after Professor Atkin's team had success with these treatments at the cellular level. Through this process, Laird's team is identifying which of these compounds is most protective against MND, requiring further in-depth study in ongoing investigations.



CELLULAR BIOLOGY AND THERAPEUTICS TEAM

Cellular discoveries lead to drug targets

By discovering processes in cells that cause MND, researchers can identify new drugs to slow or stop this degeneration.

Over the last ten years, the Cellular Biology and Therapeutics team led by Professor Julie Atkin has progressed from discovering processes at the cellular level that cause MND, to testing two new drugs on cells, zebrafish and then mice, with a third one in progress. Patents for these therapies are pending approval.

"We've seen that these drugs are protective in mice and prevent their motor neurons from dying," says Atkin. "The drugs also improve the motor performance of these animals, so that's quite exciting."

Atkin is co-director of the MND Research Centre and internationally recognised for her research on cellular mechanisms leading to neurodegeneration in MND.

Her team is collaborating with chemists at La Trobe University in Melbourne to ensure the pharmacological properties of these drugs are tolerated well in humans as well as mice.

"Once we've modified these drugs, we will test them again in animals, so hopefully some of these drugs may eventually make it into human clinical trials," she says. "This is always a long journey and most drugs do not make it past this stage."

CELLULAR DISCOVERIES

Over the last decade, Atkin's team has focussed their cellular research on pinpointing the first things that go wrong in MND so that they can target drugs to prevent the disease progressing at the early stages.

"It's a natural progression to develop therapies based on the disease mechanism. We're trying to find the most upstream mechanism because we believe this has the greatest probability of success as a drug target," says Atkin.

Some of the team's significant discoveries include identifying that DNA damage is present in MND, and that the most important protein linked to MND, TDP-43, is a protein that normally repairs DNA.

They've also identified the function of another protein, C9orf72, that when mutated causes familial MND, commonly passed down in families. This protein is normally required for cellular transport and in processes that cells use to get rid of damaged proteins.

Her team also has discovered a new form of protein called FUS, that is unusual amongst the proteins linked to MND because it is found outside the cell rather than inside. This protein seems to aggregate a lot more than other proteins usually associated with people who have MND and also in some rare cases of people with frontotemporal dementia.The team received a National Health and Medical Research Council grant to further investigate this protein.

An important tool in the team's research is a new high-content microscopy system, the first of its kind in Australia, which enables her team to examine and analyse cells very rapidly. "It allows us to automate our analysis, which is a lot faster than doing it manually," she says.

The team are also using samples from the Neurodegenerative Disease Biobank to investigate MND's heterogeneity – the different ways in which MND manifests itself in every patient.

CELLULAR BIOLOGY AND THERAPEUTICS TEAM

BIO-TECH TO MND

Atkin completed her PhD in Molecular Biology and Biotechnology at the University of Sheffield, UK, supported by funding and a placement with Celltech, a UK biotechnology company. Her previous work focused on both immunology and neuroscience. She also spent four years working in industry at an Australian biotech company discovering new drugs for cancer and immune diseases.

Group Leader
Professor Julie Atkin*

Postdoctoral Research Fellow
Dr Mariana Brocardo*
Dr Cyril Jones-Jagaraj*
Dr Sayan Saravanabavan*
Dr Sonam Parakh*
Dr Sina Shadfar*

Research Officer
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Research Assistant
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PhD students
Zeinab Takallo Bighash*
Fabiha Farzana*
Sara Assar Kashani*
Shashi Gautam*

MRes2 student
Naima Mumtaz

** Pictured*

MULTIDISCIPLINARY
MND SERVICE AND CLINIC

Unparallelled care doubles MND patients' survival rate

Treating 1,000 MND patients in a decade, the Multidisciplinary Service and Clinic is the largest in Australia.

At any one time, the Multidisciplinary MND Service and Clinic is helping 175 people living with MND and their families throughout Australia. Established in 2010, it assists patients from early diagnosis through therapeutic trials, multidisciplinary care and end-of-life care.

"We're very fortunate to have an exceptional team of clinicians working with us," says Dominic Rowe, Foundation Professor of Neurology in the Faculty of Medicine and Health Sciences at Macquarie University. "Receiving this care doubles the patient's survival rate and dramatically improves their quality of life."

Patients visit every three months for consultations with either a physiotherapist, speech pathologist, dietitian, occupational therapist, social worker, clinical nurse consultant, genetic counsellor, respiratory physician and with Rowe himself, the neurologist who runs the clinic.

Costing $500,000 a year to run, the clinic operates entirely on donations cares for patients in Sydney, regionally or interstate, also using telehealth to widen access.

Through donations, the clinic has just bought a new Quanterix Simoa, a special machine that enables clinicians to measure markers related to nerve damage. Previously, it had to send MND patient blood samples to Sweden to have them tested.

All patients and their families are invited to participate in the Neurodegenerative Disease Biobank. The majority of patients have sporadic MND, but the clinic currently cares for 80 families that have a faulty gene that causes MND.

There are now more than 40 genes known to cause inherited MND, and families have access to in-house genetic counselling at no cost. These families can also access IVF to prevent MND in the next generation.

The clinic uses its charitable fund to pay for patients without private health insurance to be admitted to the MUH when appropriate so that they can have continuity of care.

"We've had three babies born to our Clinic over the last four years where one of the parents has a faulty gene," says Professor Dominic Rowe.

"With preimplantation genetic diagnosis and IVF, we know for certain that the babies do not carry the faulty gene and will never get MND. It's the only instance in Australia and one of the few instances in the world where families have been cured of MND."

MULTIDISCIPLINARY MND SERVICE AND CLINIC STAFF

Clinical Neurologist and Researcher
Professor Dominic Rowe*

Clinical Nurse Consultant
Kristina Barnes*

Clinical Trials Coordinator
Richard Gan

Paula Ordonez Artunduaga

Speech Pathologist
Sally Pittendrigh*

Dietitian
Meaghan Joyce*

Occupational Therapist
Kylie Christel*

Physiotherapist
Kate Bradbury*

Social Workers
Elizabeth Hannan
Christie Charlin

Genetic Counsellors
Rosie Fell*
Ashley Crook

Respiratory and Sleep Physician
Alex Dollman*

MND advisor from MND NSW
Kristie Stamford

Research Assistant
Umut Rende*

** Pictured*

TRIALLING SUCCESS

The clinic is the epicentre for the MND Research Centre's clinical trials. Macquarie is the only site in Australia in the ATLAS study, an international trial of a novel gene therapy in patients with an inherited mutation of the SOD1 gene.

"In this study, we treat these patients before they've developed MND," Rowe says. "We follow them with monthly blood tests and as soon as we see any indicator of disease activity, we start patients on treatment, two to five years before they feel weakness in a muscle and they've lost 70% of the nerve cells talking to the muscle."

By starting early treatment with a drug called Tofersen, he says this will slow the progression of the disease. "This turns survival into years rather than months," he says. He cites two patients who started the treatment in November 2021. "With the natural progression of the disease they shouldn't still be with us but they are actually going well."

The clinic has also completed a trial for 3K3A-APC in MND, an intravenous therapy that has both anti-inflammatory and neuro-protective effects. This novel therapy was trialled in a small cohort of patients. The MND Research Centre is in the middle of analysing that data.

Other patients with sporadic MND are participating in another international study: the Lighthouse 2 Trial, an international Phase 3 trial, that's repurposing the antiretroviral therapy Triumeq - also used for people with HIV. This trial will determine whether antiretroviral therapy is able to slow the progression of sporadic MND.

"The genesis of the trial started with research I was involved in 2016 with Professor Julian Gold (from the University of Sydney) and seven years later it's now a global study," says Rowe.

The clinic has also developed and patented a new blood test to diagnose MND and differentiate it from Parkinson's disease. The blood test reflects the biological process involved in the disease and may provide some more accurate measure of the disease's response to treatment.

Costing $500,000 a year to run, the Clinic operates entirely on donations.

NEUROCHEMISTRY AND MOLECULAR THERAPEUTICS TEAM

New company to translate research into therapy

Researchers are developing a new gene therapy for MND.

Backed by a newly-launched Macquarie University spin-off company (Celosia Therapeutics), Professor Roger Chung and his team are developing a patented gene therapy for the treatment of MND. They are currently in pre-clinical development in preparation for human trials and commercialisation.

Led by Chung, the Neurochemistry and Molecular Therapeutics team has created a gene therapy that targets the abnormal accumulation of the TDP-43 protein that causes MND.

Recognising the exciting potential of this novel therapy and the commercialisation steps required to take this technology forwards, Macquarie University launched a spin-off company called Celosia Therapeutics in October 2022. The company is now supporting Chung's team and another team at the University who are also developing gene-therapy solutions for neurodegenerative diseases.

Chung is the Professor of Neurobiology and Neurochemistry, and also Deputy Dean (Research & Innovation) in the Faculty of Medicine, Health and Human Sciences. He's also Chief Scientific Officer and co-founder of Celosia Therapeutics.

"The University's financial backing is greatly accelerating our research because we are now moving beyond academic research and into commercial therapeutic development," he says. "It's enabling us to transition our therapies from the lab using animal models to the clinic and develop the most effective ways to administer our therapies safely to patients in human trials."

PATIENT-CENTRED RESEARCH

In a pivotal discovery during her PhD research, Dr Stephanie Rayner found that experimentally over-expressing a therapeutic variant of Cyclin F above normal levels could target TDP-43 and prevent MND-like neurodegeneration.

"We found Cyclin F can help recycle abnormally accumulating (stuck) proteins," Rayner says. "This is an important discovery because it suggests that Cyclin F could be used therapeutically to prevent TDP-43 from getting stuck and prevent the neurons from getting sick with MND."

Visiting the Multidisciplinary Clinic and Service motivated Rayner to achieve more in her research. "Meeting MND patients face-to-face was a really good experience," she says. "There can be a major disconnect between the lab and the patient, so actually meeting people and hearing about how they were living with the disease first hand meant so much."

Rayner's findings, published in 2022, led Chung's team to develop the potential gene therapy, apply for multiple patents and to seek to commercialise the research. "Our challenge was to develop a comprehensive gene therapy that addressed all the key TDP-43-linked disease mechanisms," Chung says.

A digital micrograph of a motor neuron from a postmortem sample from a MND patient. The green 'tendrils' are abnormal accumulations of TDP-43. Image captured by Rowan Radford.

CREATIVITY AND INNOVATION UNDERPINS THE SOLUTION

A key aspect of the team's work is the continual innovation of the technology. The team has bioengineered a set of therapeutic enhancements into cyclin F. This includes variants that focus targeting solely onto TDP-43, variants that direct Cyclin F to specific parts of the cell for localised activity and shortened variants which provide different therapeutic functionalities.

Their most recent advance is the development of a switch that regulates the gene therapy: this turns on therapeutic gene expression when abnormal TDP-43 levels accumulate and turns off when normal TDP43 levels are restored. This creates a potentially unique, one-shot self-regulating gene therapy.

NEUROCHEMISTRY AND MOLECULAR THERAPEUTICS TEAM MEMBERS

Group Leader
Professor Roger Chung*

Group Leader
Dr Albert Lee

Group Leader
Associate Professor Marco Morsch*

Research Fellows
Dr Pradeep Cholan*
Dr Jennilee Davidson*
Dr Livia Rosa Fernandes*
Dr James Hilton*
Dr Alison Hogan*
Dr Luan Luu*
Dr Cindy Maurel*
Dr Stephanie Rayner*
Dr Grant Richter*

Research Assistants
Flora Cheng*
Tyler Chapman*
Rowan Radford*

PhD Students
Afshin Babazadeh*
Hannah Suddull*
Paulina Szwaja

** Pictured*

PATH TO GENE THERAPY

In 2008, Professor Ian Blair, together with national and international collaborators, made the seminal discovery of mutations in the TARDBP gene (which encodes TDP-43 protein) in some Australian MND patients (and patients worldwide) – revealing the TDP-43 protein as the key player in the disease. In 2016, Blair's Genetics and Genome team discovered mutations in the CCNF gene (which encodes Cyclin F protein) in MND patients and Chung's team embarked on research to understand how that gene caused motor neuron degeneration.

Since then, drawing on expertise in protein chemistry, biochemistry and molecular biology, cell biology and experimental disease models, Chung's team has revealed more about the role of Cyclin F in MND. They found it's a key component of the intracellular pathway responsible for clearance of proteins. Importantly, they found that Cyclin F binds to TDP-43 and regulates its degradation.

MORE ABOUT THE NEUROCHEMISTRY AND MOLECULAR THERAPEUTICS TEAM

Our focus is to understand the molecular cause of MND, and to use this knowledge to develop new therapeutic strategies. We focus on harnessing endogenous neuroprotective pathways, using molecular and synthetic biology tools to intelligently modify and deliver proteins with enhanced therapeutic capabilities.

NEUROIMAGING AND DEGENERATION TEAM

Zebrafish provide clues for how proteins clump in MND

Using fluorescent markers, researchers label motor neurons in zebrafish to understand why damaged proteins clump together and spread to other cells.

Associate Professor Marco Morsch's Neuroimaging team works with zebrafish to visualise how MND disease proteins clump together within nerve cells, how they circulate throughout the nervous system and how this process can be targeted to help people living with MND.

"We call this process the 'molecular grammar' of the cell, this means the fundamental drivers that regulate the hallmark protein in MND, TDP-43, how it moves, how it clumps," Morsch says. This abnormal behaviour of the TDP-43 protein, seen in almost all patients, is central to the pathology of MND.

His team also focuses on why the proteins clump together in a very short timeframe in people with MND, without needing to go through - or escaping - normal regulatory processes.

"We now believe that when people have this clumping, but no other clinical signs, then this may be a precursor for disease-related pathology," Morsch says. "The transition of liquid-like proteins to become more solid might be a fundamental first step of how these aggregates occur in disease."

MARKING FISH

Because zebrafish embryos and juveniles are transparent, researchers use fluorescent markers in the fish to label the proteins and motor neurons and use microscopes to observe how MND develops and spreads within these nerve cells.

"I remember the first time when I saw the fluorescent labels in a fish and cells moving around within a living organism - absolutely fascinating," says Morsch. "We watch in real time, how motor neurons respond to the disease and how the cells in the brain and spinal cord battle these disease aggregates."

Over the last year, Morsch has received a grant from the National Institute of Health, one of the largest research funds in the US, which enabled him to expand his team and hire post doctoral researchers.

Morsch's team has also identified the critical role of a particular immune cell called microglia. These microglia cells normally clear dying nerve cells and disease aggregates so that the disease proteins can't spread to other cells.

"When we experimentally interfere with them," Morsch says. "These microglia cells help to reshape, rewire these neurons to make sure that this is not a complete failure of the system just because one cell dies. They actually try to detour around the normal paths and form new circuitries."

In another project in conjunction with Professor Roger Chung's Neurochemistry and Molecular Therapeutics team, Morsch's team is looking at how they can use this information to deliver particular therapeutic medications and compounds to target MND and measure how much of the compound needs to cross the blood-brain barrier.

Overall Morsch believes that zebrafish provide researchers a fast track to test compounds and assess how they affect critical mechanisms.

NEUROIMAGING AND DEGENERATION TEAM GROUP MEMBERS

Group Leader
Associate Professor Marco Morsch*

Senior Lecturer
Dr Emily Don

Research Fellows
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Dr James Hilton*
Dr Cindy Maurel*
Dr Pradeep Manuneedhi Cholan*
Dr Luan Luu*
Dr Grant Richter*

Research Assistant
Tyler Chapman*
Rowan Radford
Kelly Foskett

PhD Student
Andres Vidal-Itriago
Natalie Scherer

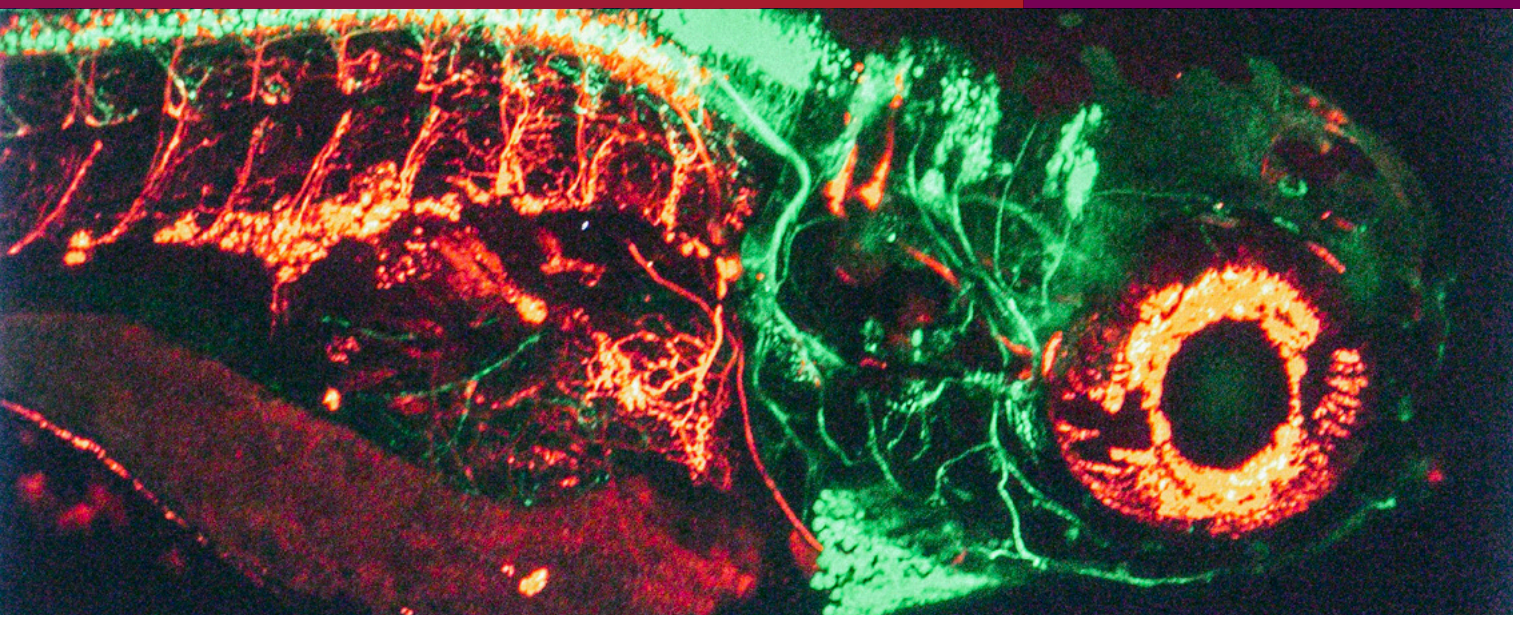
** Pictured*

SWITCH FROM NEURONS TO CELLS

Morsch is Co-Director of Research at the Macquarie Medical School with Associate Professor Kelly Williiams, overseeing the research of 350 staff and students. In 2018, he was awarded the Outstanding mid-career researcher prize by MND Research Institute of Australia.

The MND Research Centre at Macquarie recruited him in 2014 and he switched his focus from nerve-muscle connections to the main cell body and how it's affected by disease. At the MND Centre, he also got to work with zebrafish for the first time. During his first four years at the Centre, Morsch worked as a researcher with Professor Chung.

By 2018, it was a natural progression that Morsch's team would split off into a discreet team - particularly after receiving external recognition from grant funding agencies and making seminal contributions to his research field.



NEUROPROTEOMICS TEAM

Proteins link to MND's cause

Researchers are moving towards discovering how to manipulate proteins to halt motor neuron defects

Dr Albert Lee leads the NeuroProteomics Research Team at the MND Research Centre. Proteomics is the study of how all proteins function and interact with each other, to perform their functions in cells.

In a healthy person without MND, TDP43 proteins stay inside the nucleus.. However in more than 98% of patients with MND, the TDP43 moves outside the cell's nucleus to form clusters. Lee's team found this abnormal behaviour alters normal protein pathways and prevents repair within cells.

Lee's team has identified some key proteins involved in the initial stages of this MND-specific protein 'aggregation' or clumping.

"We are trying to determine how potential causes, such as gene mutations or stressors, affect proteins, how these defects make the protein toxic, and how it affects the motor neurons that ultimately cause MND," Lee says. "Compared to other areas such as cancer, applying proteomics in MND is still in its infancy and has not been studied much globally. The Centre is at the forefront of this new research."

ROAD TO MND

After finishing his PhD at Macquarie University, Lee worked at the New York University School of Medicine in the US as a proteomics scientific officer. He then completed a three-year postdoctoral research fellowship at the Johns Hopkins University School of Medicine in Baltimore.

In 2014, when Professor Roger Chung was looking for a proteomics scientist to join his team at Macquarie, Lee fitted the bill. His mandate as a post doctoral research fellow was to develop an independent research program to bridge the infrastructure capabilities at the Australian Proteome Analysis Facility (APAF) and conduct clinical and medical research in the Centre.

Although initially Lee was part of the team led by Chung, his research grew exponentially. By natural progression, Lee formed his own independent proteomics group in late 2019 and he now works with a staff of six researchers.

"I was the glue linking Professor Blair's genes and genetics group to Professor Chung's group," Lee says. "Now that's evolved and my team has become arguably the go-to place nationally for researchers and even drug companies to answer questions on proteomic research in new and degenerative diseases."

TEAM DISCOVERIES

Lee has been part of many of the significant discoveries at the Centre including the research by Professor Ian Blair and Associate Professor Kelly Williams published in 2016 that discovered that a mutated version of the CCNF gene in MND patients causes defective tagging of TDP43, marking it for retention instead of for recycling.

Lee's team has also discovered one important proteomic pathway that prevents MND-specific protein clumping. "This gave us an idea of how we can use this clearance pathway to our advantage and stop MND-specific proteins sticking together and causing MND," he says.

He was also involved in the research published in mid-2022 with post doctoral student Dr Stephanie Rayner when they identified a way to force the body to break down TDP43 using another of its naturally occurring proteins called cyclin F.

TAKING THE WEIGHT

Lee's team uses a mass spectrometer for a lot of their analysis. It measures the mass of molecules at rapid speed, such as proteins made by cells that may cause MND. This enables researchers to capture a snapshot of the cellular or disease state.

"We're trying to holistically understand the dynamic changes that occur during stress and survival of a cell with MND gene mutations, to further develop hypotheses and provide in depth knowledge," Lee says.

Using this information, his group then works with other teams in the Centre to explore ways to remove these toxic proteins and hopefully restore or minimise the amount of damage to the neuron.

NEUROPROTEOMICS TEAM MEMBERS

Group Leader
Dr Albert Lee*

Research Fellow
Dr Livia Rosa Fernandes*

Postdoctoral Research Fellow:
Dr Stephanie Rayner*

Postdoctoral Research Associate
Dr Jennilee Davidson*

Research Assistant
Flora Cheng*,
Tyler Chapman*

PhD Student
Hannah Suddull*

MRes Student
Selina Zhang*

** Pictured*

Next generation researchers

More than 90 researchers across seven teams work in the MND Research Centre. Some of them discuss what motivates them.

DR JENNILEE DAVIDSON: After majoring in Biology at Queen's University in Canada, a stint at a traumatic brain injury clinic, then a Masters at York University, Davidson came to Australia to do a PhD with Professor Roger Chung's team. "Science has always been a natural curiosity of mine," she says. Her current post doctoral work with Dr Albert Lee combines proteomics techniques with biochemical experiments in cell models to examine protein interactions and modifications to see how that affects cells of MND patients.

"It's such a tricky disease to understand at the cellular level. Trying to piece that puzzle together, really fascinates me. The Centre has such a multi disciplinary approach that brings together so many different perspectives to find a cure."

In **DR SONAM PARAKH'S** extended family, everyone is in medicine. "I decided my career direction very early on in life," she says. After a Bachelor's in Biotechnology at MS Ramaiah University in India, she completed a Masters and PhD under Professor Julie Atkin at La Trobe University in Melbourne. When Atkin moved to Sydney to establish the Centre, Parakh followed suit.

"I realised that this was a golden opportunity, with all the best MND researchers in Australia coming together to collaborate and to have resources all in one place," she says. "I wanted to be part of it."

Parakh is looking at the role of molecular chaperones and their interaction with proteins affected by MND. She's determining how the chaperones can reduce diseased protein clumping, and is also part of Atkin's project testing therapies on these cells in patient tissues and mice.

DR CINDY MAUREL has worked with Dr Marco Morsch's team for more than two years. Starting with an undergraduate Chemistry degree and a Master in Biochemistry in the University of Toulouse in France, Maurel moved into Neuroscience with a PhD in Tours.

"I had come from a different background than other students, but I started to get really fascinated by the complexity of the nervous system and how little we really knew about it," she says.

Maurel jumped at the opportunity to join Morsch's team to continue to study MND as a postdoc, as she'd worked on the misregulation of TDP43 protein in her PhD. Now she works with zebrafish and fluorescent markers. "It's like watching CCTV and seeing what happens to the fish in real time rather than in a static state. Fantastic!"

TYLER CHAPMAN studied a Bachelor of Advanced Science with Honours at the University of NSW, specialising in Genetics and Biotechnology. "I thought the concept of designing biology and DNA was incredible," he says. After graduation, he worked with the Walter and Eliza Hall Institute (WEHI) of Medical Research in Melbourne.

When COVID-19 hit in 2020, he returned to Sydney and found his current role at the Centre working with Associate Professor Marco Morsch and Professor Roger Chung developing a method to deliver an MND therapy.

His research focuses on a process similar to the COVID vaccine, based around the Adeno-Associated Virus (AAV) – a delivery system which tells a patient's cells to make certain proteins for the body to learn to fight it. "In our case, we can tell the cells to make a specific MND therapy on their own with introduced DNA," Chapman says.

When a close high school friend's father died of MND, this had a big impact on doctoral candidate **KATIE ROBINSON** "I had first hand experience of seeing how rapidly his dad deteriorated over a couple of years and how it also affected family members and friends," she says.

After completing a Bachelor of Medical Science, she met Dr Angela Laird at the Centre in the first rotation of her Masters by Research and became intrigued with her work. Robinson is now working on her PhD and leads Laird's mouse research and tests therapies.

"As scientists, we sometimes lose sight of the big picture," says Robinson. 'At the Centre, I love how it's all about finding anything we can do to offer MND patients and their families some benefit and hope."

DR LYNDAL HENDEN completed her Bachelor of Science in Mathematics and Statistics at Massey University in New Zealand and then decided to apply her mathematical skills to medical data. She completed her PhD at the Walter and Elizabeth Hall Institute of Medical Research (WEHI) in Melbourne and developed statistical methods to identify cryptic relatedness in the human genome and the genomes of microorganisms that cause disease.

"I love working with real people's data", Henden says. "My way of helping individuals is by looking for patterns in their data, finding relatives and learning more about disease. I find that really exciting."

In 2018, she joined Associate Professor Kelly Williams' team at the Centre, to apply her methodology and algorithms to MND. Henden is now a senior postdoctoral research fellow working on various projects, using hundreds of terabytes of data collected from genomics projects patients globally.

DR ALISON HOGAN began her career in science as a veterinarian. She completed her training at the University of Sydney in 2004 and then practised for eight years. "I got really burned out," Hogan says. "It was emotionally draining and I really needed a new change and a challenge. Human medicine fascinated me, particularly neuroscience, so I followed my curiosity."

Hogan enrolled in a Masters by Research at Macquarie. In her rotations, she discovered the MND Research Centre. "Once I learned about MND, what a horrendous disease it is and met a few patients, it was hard not to get intrigued and obsessed about trying to do something about it," she says.

She completed her PhD working with Professor Ian Blair and Associate Professor Marco Morsch studying genetics of MND cell culture and zebrafish models and is now into the fourth year of her postdoctoral work.

Tragedy to triumph: a personal journey with MND

Gill Truman was diagnosed with MND a decade ago. She turned her personal tragedy into triumph by creating a charity to raise funds for research.

Gill felt a weakness in her hand while she was hanging out the washing one day at home in London. The then 30-year-old Australian-born occupational therapist had recently given birth to her second son and was on maternity leave. It was 2012.

After rounds of testing, Gill was diagnosed with Motor Neuron Disease. Within a year, she and her husband Matt and two sons returned to her hometown of Bowral in Australia for the emotional and physical support she needed.

"At the time I was diagnosed, there was no treatment, medication or drug trials for MND. Just an average life expectancy of two to five years," Gill says. "MND steals your independence and ultimately your life. That's a pretty confronting thought when you're a young mum nursing your little baby. It was devastating to think I wouldn't see my children grow up."

TRAGEDY INTO TRIUMPH

Gill became a patient of Professor Dominic Rowe at the Multidisciplinary MND Service and Clinic. She is also participating in the Lighthouse 2 Trial, an international Phase 3 trial testing a novel antiretroviral therapy for MND.

Rowe is very positive about Gill's progress on the therapy. "Over the last 18 months, her MND symptoms have slowed rapidly and we're really happy about how she's going," he says.

Gill is equally effusive about Rowe. "He is a very compassionate person and I know he will be in my life forever now," she says.

In 2015, Gill and some high school friends formed a charity to fundraise for MND and called it MotorOn. To date the charity has raised over $1.6 million for MND research, most recently holding a ball in July 2022 attended by 280 people.

DEGENERATIVE DISEASE CHALLENGES

Although her disease is not as aggressive as it could be, Gill faces the devastating consequences of living with a degenerative disease.

"You move swiftly from independence to dependence. You grieve for every loss from something big like your career to something small like not being able to take a photograph," she says. In 2019, she had to stop driving. She now uses a wheelchair and a walking frame to move around. Carers take care of her as well as her family.

Gill is dysarthric: she speaks slowly and with a severe slur. She uses eye movements to type on her computer.

She's concerned about how having a mother with MND affects her sons. "I often wonder if me having MND is going to screw them up," she says. "The good thing is I can't yell at them, of course, I'd love to run around like a whirlwind doing everything for them, but I can't. Our lives have to be so much more planned and orchestrated."

Even in primary school, the boys learned how to cook dinner, wash and iron their school clothes, becoming highly independent.

Gill attends as many of their school and sporting events as possible and is a passionate supporter from the sidelines in her wheelchair.

"Ten years ago I was upset to imagine that I wouldn't see my sons start preschool," she says. "And here I am with our eldest starting high school this year. In a funny way, I probably spend much more time with them than I ever could have without MND and I am very grateful for that."

Funding to eliminate MND

Fiona Pearce died from MND but her husband Hamish is now fundraising for a cure.

Amidst the fireworks at McMahons Point on the night of the Sydney Olympics closing ceremony in 2000, Hamish Pearce and his partner Fiona got engaged. They had met in the mid-90s on a boat in the idyllic tropical setting of the Whitsundays. They married in 2001.

In 2005, while pushing their two-year-old son Will in his pram close to home, Fiona tripped and fell. That afternoon a doctor friend looked at her grazed leg. "Fiona told her GP friend she had a gammy leg, which I thought was unusual," says Hamish. "Her friend suggested she should have some tests."

Through a process of elimination, specialists discovered Fiona had MND. The neurologist who broke the terrible news to the 32-year-old was Dr Dominic Rowe, who today heads the Multidisciplinary MND Service and Clinic. He cared for Fiona throughout the progression of the disease.

After the diagnosis, Fiona, Hamish and Will travelled to New York and New Zealand. "We tried to fit in as much as we could while she was still healthy. We did the best we could to give her the best life that she had left," he says.

Fiona worked at Macquarie Bank and was a loving mother and partner who extended that care to her friends and family. "She was a counsellor to some of her friends who were going through a hard time, not as a professional, but as a shoulder to cry on and a listening ear, " Hamish says. "She was a very caring, generous, thoughtful person."

They moved closer to her parents so Fiona could have more support. Hamish's sister moved in to help care for her.

Hamish joined forces with two friends and formed the MonSTaR Foundation in 2007. The charity now supports MND research and educational programs for children with disabilities and special learning needs.

To raise money for these causes, MonSTaR started holding annual Golf Days at Pennant Hills Golf Club with about 140 golfers taking part, which then extended into special cocktail parties, dinners and gala balls at the club and for several years, in the city.

"Fiona came to that first event to kick things off, which meant a lot to everyone and was very emotive," Hamish says. "Unfortunately, she died just a couple of weeks later." Since then, MonSTaR has held 14 events and raised more than $4.3 million.

"We're very lucky that we are in a position to give to these causes and make a small difference," Hamish says. "My hope is that one day we don't have to fundraise for MND anymore because they've found a cure."

Harnessing an integrated discovery and evidence-based clinical program to deliver advances in patient outcomes and improve the lives of MND patients and their families.

MACQUARIE University
SYDNEY·AUSTRALIA

MOTOR NEURON DISEASE RESEARCH CENTRE

Events

MND GALA 2022

After a hiatus because of COVID19, we held our MND Gala at the Art Gallery of NSW in 2022. More than 350 guests enjoyed champagne and hors d'oeuvres while viewing the magnificent art from the Archibald exhibition.

Our live auction was a particular highlight. Professor Dominic Rowe donated a lunch for 10 at his farm getaway in Bulga, New South Wales. This caused an intense bidding war, the last 2 bidders were up to $29,000 and $30,000. Dominic announced that if the second bidder could match the first he would put on 2 lunches. Both agreed and set off a chorus of cheers.

FIRIES CLIMB FOR MND

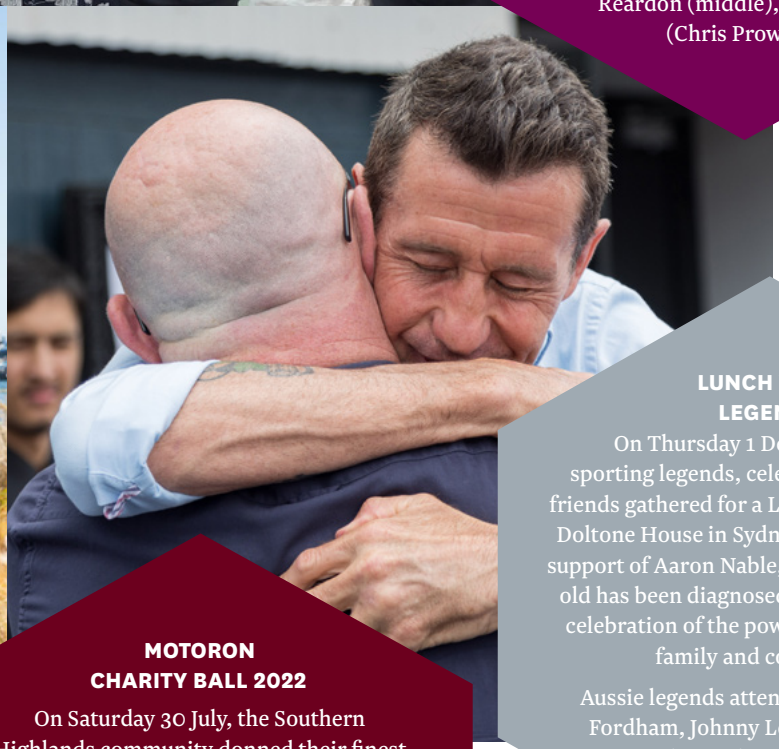
Firefighter Gavin Clifton ran up and down 951 steps at Furber Stairs in the Blue Mountains, NSW for more than 12 hours to raise money for research into MND. Gavin is preparing to run the stairs for the fifth time in 2023. His tremendous feat of trekking is truly inspirational.

ROTTNEST CHANNEL SWIM

Having recently lost his mother to Motor Neuron Disease. Crosby Radburn and his friend Ben Hooper embarked on a 20km swim from Perth to Rottnest Island, the Rottnest Channel Swim. Their team called 'Blokes Who Stroke' set themselves a target of raising $5000. They have raised over $20,000.

FIGHT MND PEDAL CURE FOR MND

Dr Lyndal Henden and Associate Professor Kelly Williams were invited speakers for the FightMND Pedal Cure 4 MND event in Temora in country NSW on 5th March. The fundraising event raised over $450,000 which goes to FightMND. Pictured - Kelly and Lyndal are with the other guest speaker, paralympian Scott Reardon (middle), and cyclist (Chris Prowse).



LUNCH WITH LEGENDS

On Thursday 1 December 2022, sporting legends, celebrities, family and friends gathered for a Lunch with Legends at Doltone House in Sydney. The lunch was in support of Aaron Nable, who at just 45-years-old has been diagnosed with MND. It was a celebration of the power and resilience of family and community.

Aussie legends attending included Ben Fordham, Johnny Lewis, Matt Nable, Andrew Johns, Matty Johns and Gary Jubelin.

MOTORON CHARITY BALL 2022

On Saturday 30 July, the Southern Highlands community donned their finest party apparel and dug deep to raise an incredible $350,000 for MND research. It is run by a group of friends rallying together to show their support for their friend Gill Truman, who was diagnosed with MND in 2012. The MotorOn Charity Ball has become a night of nights in the Southern Highlands and its success is testimony to the power of friendship.

Our Leadership Team

PROFESSOR IAN BLAIR
Centre Co-Director and Group Leader

Professor Ian Blair has a long-standing track record in research identifying and understanding the genetic and genomic factors that underlie the onset and progression of motor neuron disease (MND/ALS) and related disorders.

Contact: ian.blair@mq.edu.au

PROFESSOR DOMINIC ROWE AM
Centre Deputy Director

Professor Dominic Rowe's areas of expertise include MND and Parkinson's disease among other forms of neurodegenerative disease. As the inaugural Professor of Neurology at Macquarie University, he also researches the causes of and therapies for these diseases.

Contact: dominic.rowe@mq.edu.au

PROFESSOR JULIE ATKIN
Centre Co-Director and Group Leader

Professor Julie Atkin is interested in the basic molecular and cellular mechanisms in MND. She is developing new therapeutic strategies to prevent neurodegeneration.
Her work focuses on the role of DNA damage, cellular stress responses, redox signalling and cellular trafficking pathways.

Contact: julie.atkin@mq.edu.au

PROFESSOR GILLES GUILLEMIN
Centre Executive Member and Group Leader

Professor Gilles Guillemin is internationally recognised as a leader in the fields of tryptophan, neuroinflammation and neurotoxicity research. His team has three main interests:

- identification of environmental factors associated with MND
- developing new sets of blood biomarkers for MND progression and response to treatment
- developing therapeutic strategies for MND using new enzyme inhibitors.

Contact: gilles.guillemin@mq.edu.au

ASSOCIATE PROFESSOR ANGELA LAIRD
Centre Executive Member and Group Leader

Associate Professor Angela Laird studies the pathogenesis of movement disorders, with a particular focus on identifying and testing potential disease treatments. Her group is currently performing drug-testing studies on zebrafish and cellular models of MND and related diseases. The best therapeutic candidates
will receive further preclinical investigation to aid development of effective treatments for MND.

Contact: angela.laird@mq.edu.au

PROFESSOR ROGER CHUNG
Centre Executive Member and Group Leader

Professor Roger Chung's team explores the neurobiology and neurochemical pathways that underlie MND. His team has four main interests:

- molecular and proteomic understanding of the origins of MND
- understanding how non-neuronal cells contribute to disease processes
- developing biomarker assays for disease onset and progression
- developing therapeutic strategies for MND using gene therapies and nanoparticle-based drug delivery systems.

Contact: roger.chung@mq.edu.au

ASSOCIATE PROFESSOR ALBERT LEE

Centre Executive Member and Group Leader

Dr Albert Lee is interested in understanding cell stress responses and how impairments to this process can manifest into diseases such as MND. He uses proteomics to identify changes to the cells' proteins to capture a snapshot of a cellular or disease state. His team's work aims to discover new cell pathways that are affected in MND that may be potential targets for therapy.

Contact: albert.lee@mq.edu.au

ASSOCIATE PROFESSOR KELLY WILLIAMS

Centre Executive Member and Group Leader

Associate Professor Kelly Williams and her research team develop and apply computational and statistical methods to the genetic code of thousands of neurodegenerative disease cases from around the world. Their current research interests are:

- uncover shared ancestry in MND to pinpoint disease-causing gene defects
- machine learning to develop a prognostic toolkit for the clinic
- identify biological and genetic modifiers of MND

Contact: kelly.williams@mq.edu.au

ASSOCIATE PROFESSOR MARCO MORSCH

Centre Executive Member and Group Leader

Associate Professor Marco Morsch's team explores the basic biological mechanisms that drive neuronal communication and cell-cell interactions. A key objective is the translation of these discoveries into novel therapeutic strategies for MND/ALS. This includes the development of advanced delivery techniques of medicines to the Central Nervous System (CNS).

Contact: marco.morsch@mq.edu.au

Centre Directors
Deputy Director
Group leaders
One representative from each academic level (A-D), drawn from the Centre (by nomination for 12-month term)
One HDR student (by nomination for 12-month term)
Centre Administrator

GOVERNANCE

The key Centre leadership group is the Executive. Operational committees responsible for specific activities include the Biobank Committee, Philanthropy Committee, Senior Scientist Group, Conference Working Group and Laboratory Operations Committee.

EXECUTIVE GROUP

The Executive Group meets in person every two months, chaired by a Centre Director, to set strategic direction for the Centre and oversee operational management through the various committees listed above. The Executive is responsible for managing the Centre budget including philanthropic funds, as well as intellectual property, ethics approvals and contracts, upon the advice of respective Committees.

DIVERSITY

1 | 1

We have one female and one male co-director of the Centre.

16 | 11

We have sixteen female research fellows and eleven male research fellows.

3 : 6

Our current female to male Group Leader ratio is 3:6.

60%

Approximately 60% of our HDR students are international, providing a diverse and stimulating environment in the Centre.

Global institutional collaborators

The MND Research Centre has collaborated with 637 research institutions from all over the world in 62 countries.

AMERICA

- *Argentina*
- *Brazil*
- *Chile*
- *Mexico*
- *Uruguay*

CANADA

- *Quebec*
- *Nova Scotia*
- *British Columbia*
- *Ontario*
- *Alberta*
- *Saskatchewan*

UNITED STATES

- *Iowa*
- *Ohio*
- *Oregon*
- *Minnesota*
- *Tennessee*
- *Maryland*
- *Arizona*
- *Georgia*
- *Florida*
- *California*
- *Michigan*
- *Missouri*
- *Kansas*
- *New Hampshire*
- *Utah*
- *Virginia*
- *South Carolina*
- *Texas*
- *Wisconsin*
- *Nebraska*
- *New Jersey*
- *Alabama*
- *Washington*
- *Arkansas*
- *Indiana*
- *Louisiana*
- *Massachusetts*
- *Oklahoma*
- *Connecticut*
- *West Virginia*
- *Colorado*
- *Rhode Island*
- *New Mexico*
- *North Carolina*
- *Kentucky*
- *Pennsylvania*
- *Illinois*
- *New York*

EUROPE

- *Austria*
- *Belgium*
- *Bulgaria*
- *Croatia*
- *Cyprus*
- *Czech Republic*
- *Denmark*
- *Finland*
- *France*
- *Germany*
- *Greece*
- *Hungary*
- *Iceland*
- *Ireland*
- *Italy*
- *Luxembourg*
- *Malta*
- *Netherlands*
- *Norway*
- *Poland*
- *Portugal*
- *Romania*
- *Russian Federation*
- *Serbia*
- *Slovakia*
- *Slovenia*
- *Spain*
- *Sweden*
- *Switzerland*
- *Turkey*
- *United Kingdom*

ASIA

- *Bangladesh*
- *China*
- *Hong Kong*
- *India*
- *Indonesia*
- *Islamic Republic of Iran*
- *Iraq*
- *Israel*
- *Japan*
- *Kazakhstan*
- *Democratic People's Republic of Korea*
- *Republic of Korea*
- *Kuwait*
- *Macao*
- *Malaysia*
- *Oman*
- *Pakistan*
- *Palestine*
- *Qatar*
- *Saudi Arabia*
- *Singapore*
- *Taiwan*
- *Thailand*
- *United Arab Emirates*

AFRICA

- *Egypt*
- *Seychelles*
- *South Africa*
- *Tunisia*

AUSTRALIA AND OCEANIA

- *New South Wales*
- *Queensland*
- *Tasmania*
- *South Australia*
- *Victoria*
- *Western Australia*
- *Australian Capital Territory*
- *New Caledonia*
- *New Zealand*

Community funds - our research lifeline

Donor support and community fundraising ensure the MND Research Centre and the Multidisciplinary Service and Clinic improve the lives of people with MND.

We sincerely thank you for helping change lives, for being part of our journey and sharing our vision. We are enormously grateful and humbled by the support from thousands of donors, be they individuals, organisations, foundations or entire communities each and every year. This support is instrumental in continuing our work, exploring new research avenues, development of medications, new therapies, trials and their application in our clinic.

Many lives are impacted by this terrible disease. Everything we can do to work towards a cure is vital.

Since 2013, the Centre, Service and Clinic have received almost $13 million in philanthropic support. This has helped form the most comprehensive and all-encompassing MND research centre in Australia, where researchers and clinicians work side-by-side to decipher this disease.

No other centre has this kind of firepower to deliver the science and breakthroughs that will disrupt the trajectory of MND.

The Service and Clinic receive no federal or state funding to operate. They run entirely with the support of public donations and research grants. At the Centre, our researchers compete for grants from the National Health and Medical Research Council, the Australian Research Council and the Motor Neurone Disease Research Institute Australia, among others. It is only with adequately funded research that we can discover how to beat MND. We know it can be done – but we need your help to make it happen.

Your donations support a variety of research and clinical initiatives, including:

- identifying genetic, lifestyle and environmental risk factors to help understand why people develop MND and prevent its onset and progression
- new drug discovery and development – supporting innovative strategies to identify and develop potential new therapies
- clinical trials – allowing us to test new therapies for MND, which may slow and stop the disease
- biomarker discovery and development – tracking progression and monitoring the effectiveness of potential new drugs
- Neurodegenerative Disease Biobank – funding the continual collection, analysis and preservation of biological samples, which help us understand the causes and biomarkers of MND
- supporting early and mid-career researchers – helping us recruit and support the best researchers to unravel the mysteries of MND
- Multidisciplinary MND Service and Clinic – giving patients access to best practice subsidised MND care.

If you would like to find out how you can support the MND Research Centre and the Multidisciplinary MND Service and Clinic, please contact Macquarie University's Advancement team:

T: 1800 673 662
E: mqadvancement@mq.edu.au

Or visit
mq.edu.au/mnd
to make a donation online.

Thank you for making a difference.

Publication highlights 2022/2023

- **ALS/FTD-causing mutation in cyclin F causes the dysregulation of SFPQ**

  Rayner, S. L., Cheng, F., Hogan, A. L., Grima, N., Yang, S., Ke, Y. D., Au, C. G., Morsch, M., De Luca, A., Davidson, J. M., Molloy, M. P., Shi, B., Ittner, L. M., Blair, I., Chung, R. S. & Lee, A.
  In: Human Molecular Genetics. 30(11):971-984. (2021)

- **Association of variants in the SPTLC1 gene with juvenile amyotrophic lateral sclerosis**

  Johnson, J. O., Chia, R., Miller, D. E., Li, R., Kumaran, R., Abramzon, Y., Alahmady, N., Renton, A. E., Topp, S. D., Gibbs, J. R., Cookson, M. R., Sabir, M. S., Dalgard, C. L., Troakes, C., Jones, A. R., Shatunov, A., Iacoangeli, A., Al Khleifat, A., Ticozzi, N., Silani, V., Gellera, C., Blair, I. P. & 28 others.
  In: JAMA Neurology. 78(10):1236-1248. (2021)

- **Emerging evidence highlighting the importance of redox dysregulation in the pathogenesis of amyotrophic lateral sclerosis (ALS)**

  Jagaraj, C. J., Parakh, S. & Atkin, J. D.
  In: Frontiers in Cellular Neuroscience. 14:581950 (2021)

- **Genetic analysis of GLT8D1 and ARPP21 in Australian familial and sporadic amyotrophic lateral sclerosis**

  Chan Moi Fat, S., McCann, E. P., Williams, K. L., Henden, L., Twine, N. A., Bauer, D. C., Pamphlett, R., Kiernan, M. C., Rowe, D. B., Nicholson, G. A., Fifita, J. A. & Blair, I. P.
  In: Neurobiology of Aging. 101, p. 297.e11-297. e13 (2021)

- **Unbiased label-free quantitative proteomics of cells expressing amyotrophic lateral sclerosis (ALS) mutations in CCNF reveals activation of the apoptosis pathway: a workflow to screen pathogenic gene mutations.**

  Cheng F, De Luca A, Hogan AL, Rayner SL, Davidson JM, Watchon M, Stevens CH, Sanz Muñoz S, Ooi L, Yerbury JJ, Don EK, Fifita JA, Maria De Los Angeles Morales Villalva, Suddull H, Chapman T, Hedl TJ, Walker AK, Yang S, Morsch M, Shi B, Blair I, Laird AS, Chung RS, Lee A.
  In: Frontiers in Molecular Neuroscience 14:627740 (2021)

- **Protein disulphide isomerase (PDI) is protective against amyotrophic lateral sclerosis (ALS)-related mutant Fused in Sarcoma (FUS) in in vitro models**

  Parakh, S., Perri, E. R., Vidal, M., Sultana, J., Shadfar, S., Mehta, P., Konopka, A., Thomas, C. J., Spencer, D. M. & Atkin, J. D.
  In: Scientific Reports. 11(1):17557. (2021)

- **Flow cytometry allows rapid detection of protein aggregates in cellular and zebrafish models of spinocerebellar ataxia 3**

  Robinson, K. J., Tym, M. C., Hogan, A., Watchon, M., Yuan, K. C., Plenderleith, S. K., Don, E. K. & Laird, A. S.
  In: DMM Disease Models and Mechanisms. 14(10): dmm049023. (2021)

- **Common and rare variant association analyses in amyotrophic lateral sclerosis identify 15 risk loci with distinct genetic architectures and neuron-specific biology**

  van Rheenen, W., van der Spek, R. A. A., Bakker, M. K., van Vugt, J. J. F. A., Hop, P. J., Zwamborn, R. A. J., de Klein, N., Westra, H-J., Bakker, O. B., Deelen, P., Shireby, G., Hannon, E., Moisse, M., Baird, D., Restuadi, R., Dolzhenko, E., Dekker, A. M., Gawor, K., Westeneng, H-J., Tazelaar, G. H. P. & 176 others.
  In: Nature Genetics. 53(12):1636-1648. (2021)

- **Cyclin F, Neurodegeneration, and the Pathogenesis of ALS/FTD**

  Rayner SL, Hogan A, Davidson JM, Cheng F, Luu L, Morsch M, Blair I, Chung R, Lee A.
  In: Neuroscientist ;1073858422112018 2. (2022)

- **Genome-wide study of DNA methylation shows alterations in metabolic, inflammatory, and cholesterol pathways in ALS**

  Hop, P. J., Zwamborn, R. A. J., Hannon, E., Shireby, G. L., Nabais, M. F., Walker, E. M., van Rheenen, W., van Vugt, J. J. F. A., Dekker, A. M., Westeneng, H-J., Tazelaar, G. H. P., van Eijk, K. R., Moisse, M., Baird, D., Al Khleifat, A., Iacoangeli, A., Ticozzi, N., Ratti, A., Cooper-Knock, J., Morrison, K. E. & 65 others.
  In: Science Translational Medicine. 14(633):eabj0264 (2022)

- **Microglia morphophysiological diversity and its implications for the CNS**

  Vidal-Itriago, A., Radford, R. A. W., Aramideh, J. A., Maurel, C., Scherer, N. M., Don, E. K., Lee, A., Chung, R. S., Graeber, M. B. & Morsch, M.
  In: Frontiers in Immunology. 13:997786. (2022)

- **NEK1 and STMN2 short tandem repeat lengths are not associated with Australian amyotrophic lateral sclerosis risk**

  Grima, N., Henden, L., Fearnley, L. G., Rowe, D. B., D'Silva, S., Pamphlett, R., Adams, L., Kiernan, M. C., Mazumder, S., Timmins, H. C., Zoing, M., Bahlo, M., Blair, I. P. & Williams, K. L.
  In: Neurobiology of Aging. 116:92-95. (2022)

- **Splicing factor proline and glutamine rich intron retention, reduced expression and aggregate formation are pathological features of amyotrophic lateral sclerosis**

  Hogan, A. L., Grima, N., Fifita, J. A., McCann, E. P., Heng, B., Chan Moi Fat, S., Wu, S., Maharjan, R., Cain, A. K., Henden, L., Rayner, S., Tarr, I., Zhang, K. Y., Zhao, Q., Zhang, ZH., Wright, A., Lee, A., Morsch, M., Yang, S., Williams, K. L. & Blair I.P.
  In: Neuropathology and Applied Neurobiology. 47(7):990-1003. (2021)

- **TDP-43 is a ubiquitylation substrate of the SCFcyclin F complex**

  Rayner, S. L., Yang, S., Farrawell, N. E., Jagaraj, C. J., Cheng, F., Davidson, J. M., Luu, L., Redondo, A. G., Rábano, A., Borrego-Hernández, D., Atkin, J. D., Morsch, M., Blair, I. P., Yerbury, J. J., Chung, R. & Lee, A.
  In: Neurobiology of Disease. 167:105673. (2022)

- **The converging roles of sequestosome-1/p62 in the molecular pathways of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD)**

  Davidson, J. M., Chung, R. S. & Lee, A.
  In: Neurobiology of Disease. 166:105653. (2022)

- **The SOD1-mediated ALS phenotype shows a decoupling between age of symptom onset and disease duration**

  Opie-Martin, S., Iacoangeli, A., Topp, S. D., Abel, O., Mayl, K., Mehta, P. R., Shatunov, A., Fogh, I., Bowles, H., Limbachiya, N., Spargo, T. P., Al-Khleifat, A., Williams, K. L., Jockel-Balsarotti, J., Bali, T., Self, W., Henden, L., Nicholson, G. A., Ticozzi, N., McKenna-Yasek, D. & 29 others.
  In: Nature Communications. 13(1):6901. (2022)

- **Redox dysregulation as a driver for DNA damage and its relationship to neurodegenerative diseases**

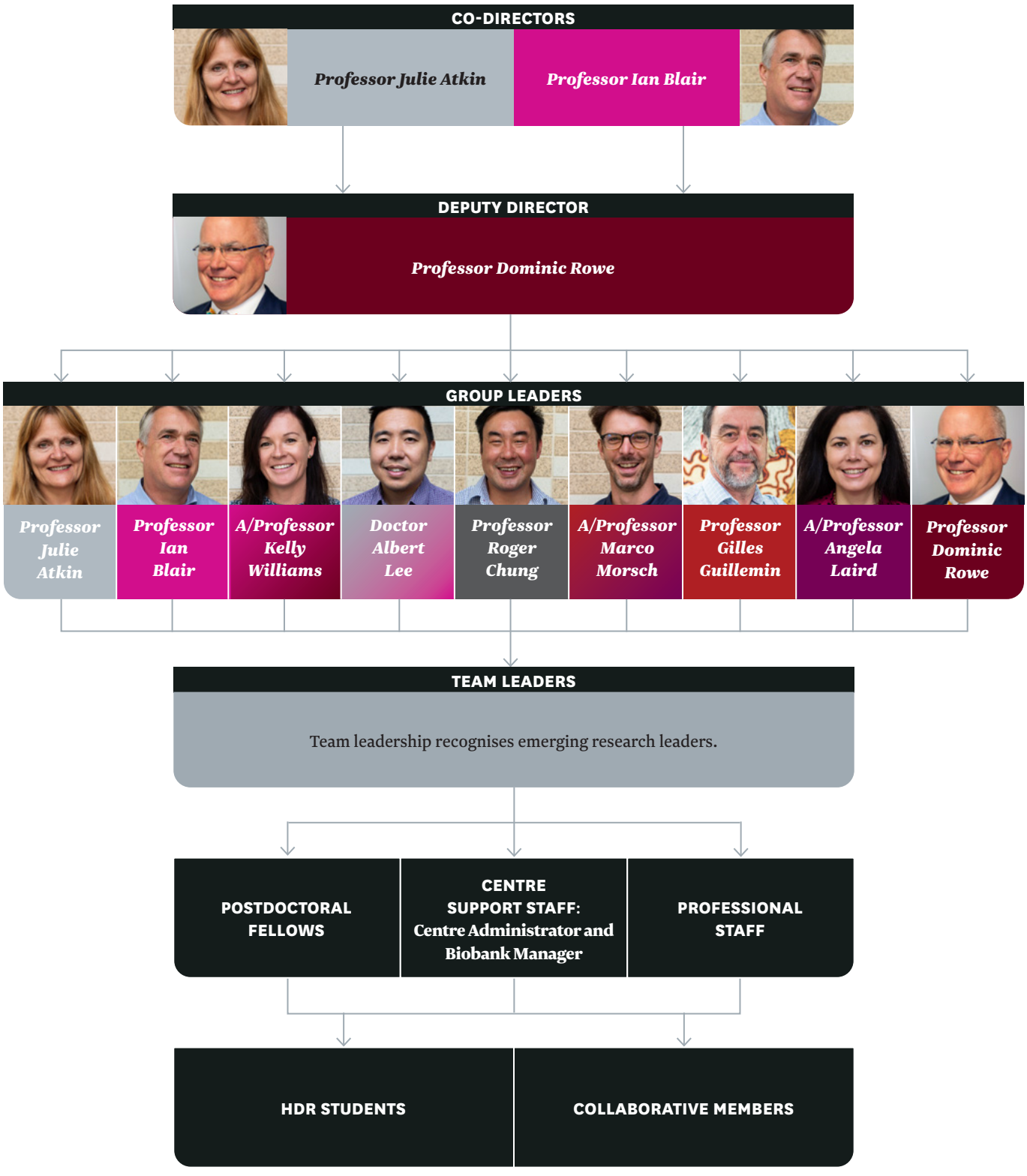
  Shadfar, S., Parakh, S., Jamali, M. S. & Atkin, J.
  In: Translational Neurodegeneration. 12(1):18 (2023)

- **Short tandem repeat expansions in sporadic amyotrophic lateral sclerosis and frontotemporal dementia**

  Henden L, Fearnley LG, Grima N, McCann EP, Dobson-Stone C, Fitzpatrick L, Friend K, Hobson L, Chan Moi Fat S, Rowe DB, D'Silva S, Kwok JB, Halliday GM, Kiernan MC, Mazumder S, Timmins HC, Zoing M, Pamphlett R, Adams L, Bahlo M, Blair IP, Williams KL.
  In: Science Advances. 9(18):eade2044. (2023)

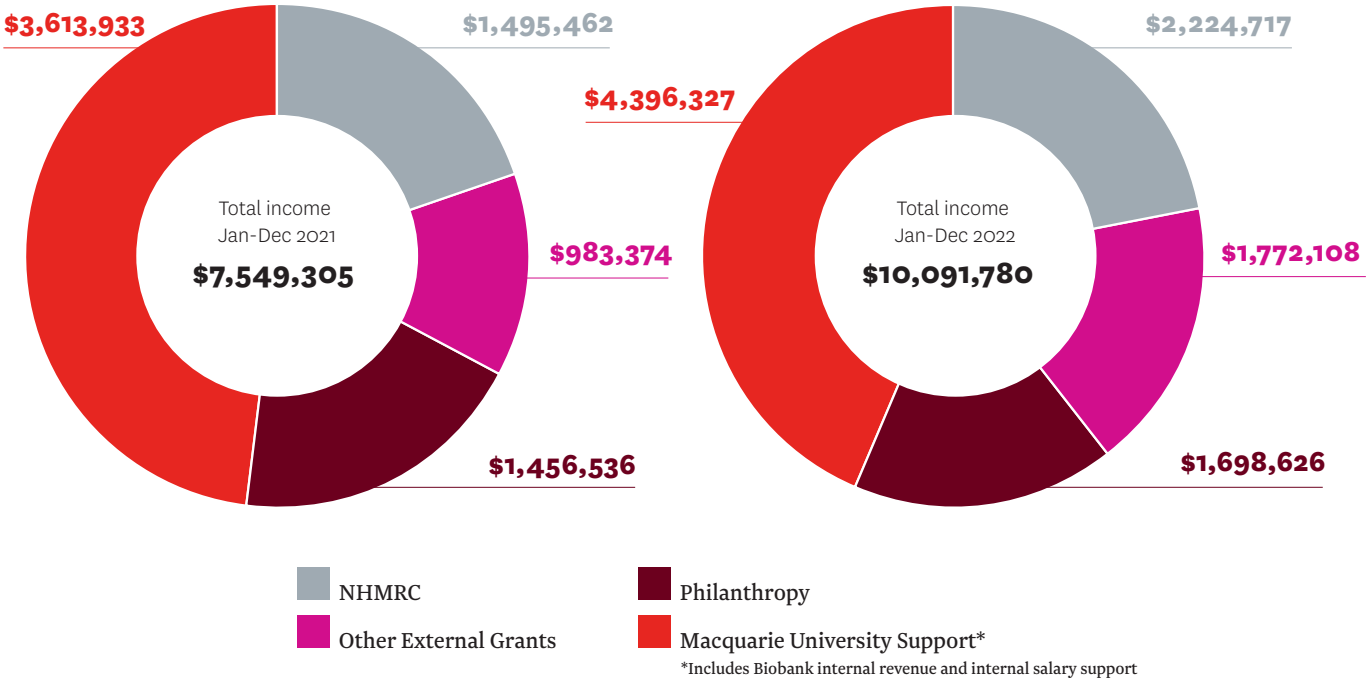
Governance structure

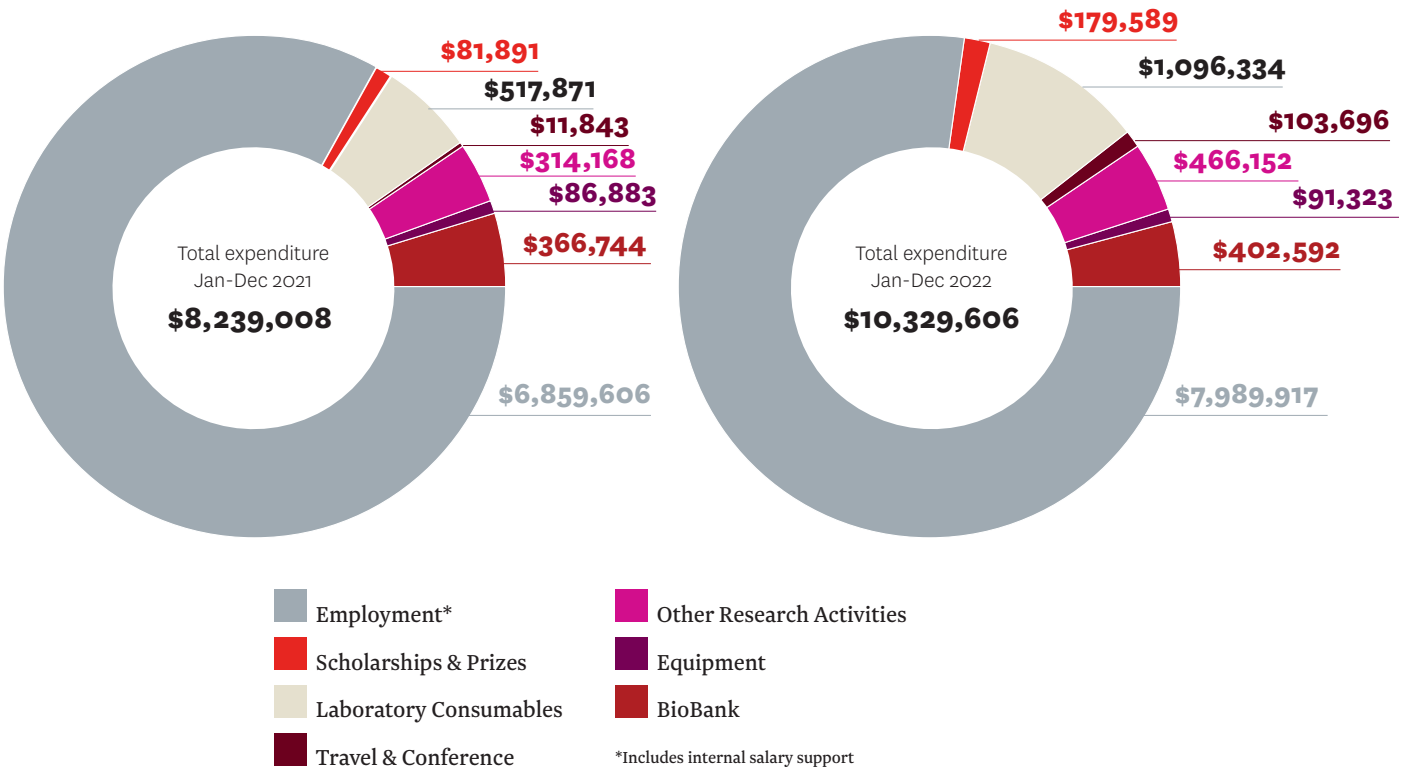
Centre leadership



Financial highlights

Summaries of the income and expenditure, in 2021 and 2022, for the MND Research Centre are illustrated below. We are immensely grateful for the philanthropic support, which is critical for underwriting scientists and sustaining the Centre's ongoing research.





Major grant highlights 2022/2023

Our researchers at the MND Research Centre receive highly competitive grants that support their salaries and research programs. Highlighted grants new and ongoing, including those from the National Health and Medical Research Council of Australia (NHMRC), are listed below. Our outstanding grant success reflects the recognition of our peers for our highly novel and innovative research programs.

Funding Body	Type of Grant	Principal Investigator	Project Title	Amount Funded	Years Funded
Hillcrest Foundation	Perpetual Philanthropic Services	Dominic Rowe	The Diagnostic Colour of Motor Neurone Disease	$70,000.00	1.5
FightMND	IMPACT Grant	Kelly Williams	Exploiting cryptic relatedness in global familial and sporadic MND to uncover disease-and-phenotype-linked genes	$250,000.00	2
FightMND	IMPACT Grant	Marco Morsch	Harnessing phase separation as a preclinical strategy for the treatment of MND	$249,996.00	2
MND Research Australia	Innovator Grant	Albert Lee	Using proteomics to reveal the components of protein aggregates to understand MND biology and identify potential therapeutic targets	$100,000.00	1
MND Research Australia	Innovator Grant	Shu Yang	Characterising CHCHD10-mediated TDP-43 mitochondria entry in MND	$100,000.00	1
MND Research Australia	Innovator Grant	Alison Hogan	RNA transport in Motor Neuron Disease - an investigation into dysfunction of the pathway and its potential for therapeutic intervention	$99,336.72	1
National Health and Medical Research Council	Ideas Grant	Angela Laird	Exploiting the neuroprotective effects of the gut microbiome for the treatment of spinocerebellar ataxia-3 and related neurodegenerative diseases	$708,205.00	3
National Health and Medical Research Council	Ideas Grant	Julie Atkin	Characterising the unique functional and pathological properties of a novel extracellular RNA binding protein in Amyotrophic Lateral Sclerosis	$810,299.00	3
National Health and Medical Research Council	NHMRC - Investigator Grants	Ian Blair	Determining the molecular basis of amyotrophic lateral sclerosis	$1,350,000.00	1
Fight MND	IMPACT Grant	Julie Atkin	EC-FUS – a novel biomarker for MND?	$249,972.00	2
National Health and Medical Research Council	Ideas Grant	Kelly Williams	When sporadic disease is not sporadic – exploiting cryptic relatedness to unravel MND genetics	$1,165,925.00	3
MND Research Australia	Innovator Grant	Lyndal Henden	Sex and ancestry – a recipe for gene discovery in MND	$100,000.00	1
US Department of Defense	ALS Research Program Therapeutic Develop-ment Award	Julie Atkin	Quinolinones as a Novel Therapeutic Strategy in ALS	US$999,748.80	3
US National Institutes of Health	Exploratory/Develop-ment Grant	Marco Morsch	In vivo characterization of the molecular drivers of biomolecular condensate formation in TDP-43 neuropathology	US$147,061.00	
MND Research Australia	Innovator Grant	Jennilee Davidson	Characterising the interactome of sequestosome-1 (p62) – the peacemaker between protein homeostasis and dysfunction	$100,000.00	1
Fight MND	Angie Cunningham PhD Scholarship	Natalie Grima/ Ian Blair	Investigating novel genomic and transcriptomic features of sporadic MND	$300,000.00	3
MND Research Australia	MND Postdoctoral Fellowship	Alison Hogan	The RNA-binding protein SFPQ offers a novel avenue to understand disease mechanisms and identify therapeutic targets in MND	$300,000.00	3
MND Research Australia	Innovator Grant	Sonam Parakh	Nucleoredoxin (NRX), a novel gene therapy target against TDP-43 multifaceted pathogenic mechanisms	$100,000.00	1
Blade Therapeutics Pty Ltd	Blade Therapeutics Pty Ltd	Angela Laird	Study of administration of calpain inhibitor compounds to mice	$95,000.00	1

Contacts

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mq.edu.au/research/mnd

ADVANCEMENT CONTACT

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Macquarie University

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Macquarie University NSW 2109

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E: mqadvancement@mq.edu.au

To make a donation, visit

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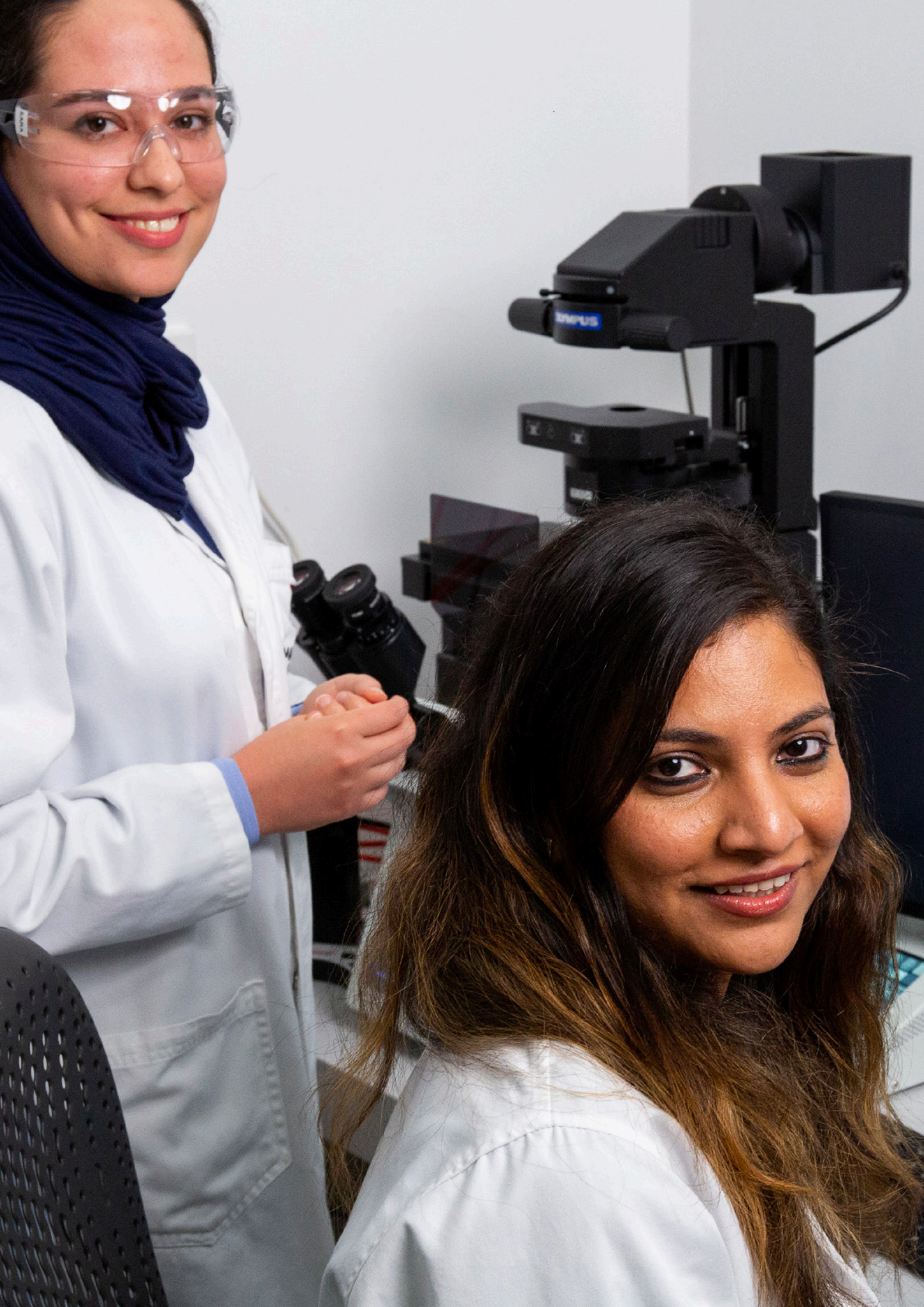
OLYMPUS