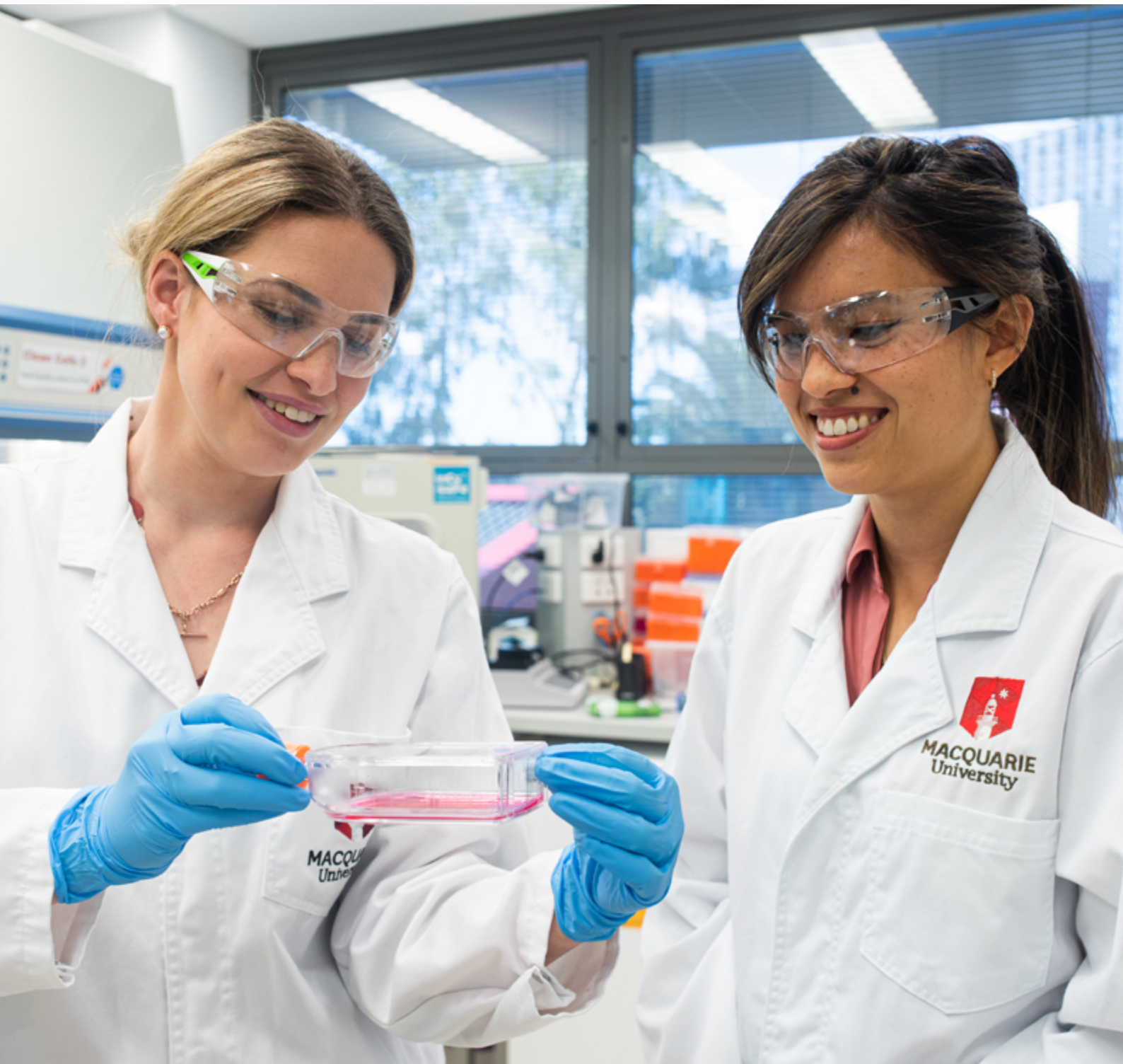


Macquarie University Centre for Motor Neuron Disease Research 2021



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 gives us great pleasure to contribute this foreword for the Macquarie University Centre for Motor Neuron Disease Research 2020-2021 report.

The Centre is an exemplar of our mission to perform high-quality research with real-world impact. As you will quickly learn from the pages that follow, the Centre undertakes outstanding research in MND as well as in related neurodegenerative diseases. Macquarie University has rapidly become widely known for MND research and clinical care thanks to the hard work and dedication of this growing team of researchers, clinician-scientists and research students.

The quality and impact of the Centre's research is illustrated in many ways, but perhaps most obviously by the award by FightMND of two of their seven Drug Development Grants for 2020 to group leaders within the Centre.

The first of these \$1 million grants was awarded to the team led by Professor Julie Atkin for a project exploring the potential of altering acting dynamics as a novel therapy for MND. The other was awarded to the team led

by Professor Roger Chung for work developing a gene therapy that will target TDP-43, the protein that is dysfunctional in almost all MND cases.

The real-world impact of the research undertaken within the Centre means that it is a flagship of MQ Health, the University's academic health science centre. 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.

The Centre for MND Research typifies MQ Health's mission because it integrates the clinical care of MND patients with leading research. As described in this report, the Centre builds on the intensely personal care delivered to MND patients to the Multidisciplinary MND Service and Clinic by creating a clinical research pipeline that characterises the patients' blood and other biological samples to understand the causes of, and develop potential treatments for, this horrendous disease.

What we find particularly exciting about

the success of the Centre is that this intersection of clinical care and research is now delivering clinical applications. For example, Professor Rowe is undertaking two clinical trials at present of potential MND therapies, testing existing drugs that are considered to have potential in MND now that we understand more of its underlying cellular and molecular causes.

As illustrated by the FightMND Drug Development Grants already mentioned, potential therapies that have been developed within the Centre are currently undergoing further development and pre-clinical evaluation. Discussions are underway with international pharmaceutical companies about potential partnerships that would be essential to take these therapies through to routine use.

It is an exciting time in MND research as we finally begin to see a glimmer of light at the end of the dark tunnel of MND. We therefore commend to you the research achievements outlined in this report and especially the Centre's vision for the next stages of research and translation in the fight against MND.

Table of contents

Introduction	1
Our vision / Our mission	2
Achievements 2020/2021	3
Top minds join MND fight	5
Our research teams	6
Frozen vaults fuel future research	7
Gene puzzles pieced together	9
Cryptic clues to MND genes	11
Hunt for biomarkers and environmental triggers	13
Pathways towards drug treatments	15
Cell biology informs drug quest	17
Clinic at the frontline in MND battle	19
Proteins unlock pathways to therapy	21
A live-stream into the brain	23
Clues to zero-in on MND's cause	25
Personal Case Stories	27-32
Events	33
Our Leadership Team	35
Global institutional collaborators	37
Community funds are vital for future work	39
Publication highlights 2020/2021	40
Governance structure	41
Financial highlights	42
Major grant highlights 2020/2021	43
Contacts	44

Introduction

In 2013, five separate and outstanding research teams took a leap of faith to relocate to Macquarie University with the collective desire to build a research powerhouse in motor neuron disease.

Central to this goal was integrating multiple scientific disciplines in a coordinated research 'pipeline' that engages patients in research. To this end, we established the Centre for MND Research, the Multidisciplinary MND Service and Clinic as part of MQ Health Neurology, and Australia's largest MND patient biobank. 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.

There are no two people who have MND in the same fashion and, in much the same way, MND affects families of people living with MND 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.

As you will see in this report, our outcomes represent a team effort. From a standing start in 2013, we are now 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. And, thank you to all of our generous donors who enable us to redouble our efforts to beat 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 2020/2021



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

Produced **> 110**

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 **> \$5.9 m**

of grants and fellowships.

Home to more than **90**

researchers working on MND.

Provided comprehensive care for **10%**

of Australians living with MND.



Conducted two clinical trials: CuATSM and the Lighthouse. The first site in the world to trial this therapy in MND. Three further trials are due to start in Q4 of 2021.

455 

Working with more than 455 global research partners.



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

Received **\$4.1m**

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.



Postgraduate student training program in MND research.

Top minds join MND fight

In 2013, researchers sharing a dream to beat motor neuron disease (MND) came together from five institutes across Australia. With complementary expertise, they built a research centre at Macquarie University.

The Centre for MND Research combined a laboratory-based research pipeline with the Multidisciplinary MND Service and Clinic 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. It was one of the first in Australia.

The new integrated centre set up Australia's largest longitudinal Neurodegenerative Disease Biobank for MND, one of the largest in the world. Patients and family members provide samples, including blood, skin, urine and hair, during regular clinic visits, all of which are stored and made available to researchers according to strict protocols. This enables the Centre to seek to understand the disease's progression over time, as well as investigate causes and therapies.

Today, the Biobank is managed by Dr Sarah Furlong, while Professor Ian Blair, Professor Gilles Guillemin, Dr Angela Laird, Professor

Julie Atkin, Professor Roger Chung, Dr Kelly Williams, Dr Albert Lee and Dr Marco Morsch lead eight research teams that collaborate on the many projects the Centre runs. They also work closely with other institutions nationally and internationally, feeding research results back into the Multidisciplinary MND Service Clinic.

Since it was created, the Centre has produced more than 300 peer-reviewed journal articles and globally participated in the identification of over 10 genes known to cause or confer risk to developing MND.

Highlights include publications in *Journal of Neurology*, *Journal of Neurochemistry* and *Science*, *Nature Communications*, *Neuron* and *The New England Journal of Medicine*. Grant success has continued, including multiple NHMRC grants and fellowships, providing more than \$5.9m in funding during financial years 2019-20 and 2020-21.

The Centre has made breakthrough discoveries

to understand MND and has multiple new potential drugs in development. The Centre has also completed two clinical trials directed by Rowe. These include the CuATSM trial and the Lighthouse Trial, which is testing a novel antiretroviral therapy for MND and is the first site in the world to do so.

Three further trials are to start in Q4 of 2021. Macquarie is the only site in Australia in the Atlas study, a trial of a novel gene therapy in patients carrying a mutation in SOD1 as the cause of MND. In addition, the WAVE study will use gene therapy in an attempt to slow the progression of MND in patients with an expansion in the gene C9ORF72. Lastly, a Phase 1 trial of a therapy termed Monepantel, an mTOR inhibitor is due to start in January 2022, funded by FightMND

The Centre also hosted the annual Macquarie Neurodegeneration Meeting, a national conference attended by more than 200 delegates in 2020 and 2021.



Left to Right: Dr Kelly Williams*, Professor Julie Atkin*, Professor Gilles Guillemin*, Professor Roger Chung*, Dr Albert Lee*, Dr Angela Laird*, Dr Marco Morsch*, Professor Dominic Rowe*, Professor Ian Blair, *pictured

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

Frozen vaults fuel future research

The Neurodegenerative Disease Biobank is the largest facility in Australia dedicated to collecting and storing biological samples and clinical data for use in MND research.

Established in 2013, the Biobank is the cornerstone of the research program at the Centre for MND research. The facility holds more than 47,000 biological samples such as blood, urine, hair or skin.

Patients attending the Multidisciplinary MND Service and Clinic are invited to participate by donating their biological samples to the Biobank. Their family members and supporters are also invited to participate, to allow 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.

“We have an unusually high participation rate compared to other biobanks,” says Dr Sarah Furlong, who manages the facility. “Participants are keen to play a role in finding the cause of this devastating disease. The reputation of the research centre is a major factor in this.”

An advantage of the Biobank being located in the same building as the Clinic is that samples can be quickly processed and stored.

In addition to samples, the Biobank collects extensive demographic, lifestyle and clinical data, which is uploaded to a dedicated content management system. This increases the power of the research immensely.

“This is critical so that we can track biological changes with clinical changes,” says Furlong. “There is a lot of variability in MND patients. For example, some are initially affected in their speech, others by weakness in one of their limbs. Some first develop symptoms in their twenties, others in their eighties.”

So far, researchers have used more than 4,200 biobank samples, integrated with data, in 25 projects across the fields of genetics, proteomics, cellular stress, biomarkers and environmental studies. These projects include collaborators across Macquarie University, nationally and overseas.

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.

PROJECT MinE

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.

Samples are also sent worldwide for analysis for numerous genetics, proteomics, biomarkers and environmental studies.





**NEURODEGENERATIVE DISEASE
BIOBANK TEAM**

Manager
Sarah Furlong*

Systems Developer
David Poynter*

Biobank Co-ordinator
Susan D'Silva*

Biobank Technician
Elisa Cachia*

Biobank Technician
Kristine Deang*

**Pictured*

PROCESSING SAMPLES

Technicians adhere to strict protocols to ensure the best possible quality of samples and data – the facility was one of the first biobanks to obtain NSW Health Biobank certification, in March 2019.

A robotic instrument 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.



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



GENETICS AND
GENOMICS TEAM

Gene puzzles pieced together

Inherited gene mutations cause about 10 per cent of MND cases. The remaining cases are sporadic and the causes unknown. Worldwide, scientists have identified more than 20 genes that cause the disease. Further investigation may lead to therapies to slow MND progression.

As leader of the Centre's Genetics and Genomics team, part of a global consortium that has identified numerous inherited genes that cause familial MND, Professor Ian Blair is keen to understand the genetic factors that account for the variability in MND. These include the age when symptoms first appear and how fast the disease progresses.

"If we can identify which genetic or genomic factors are responsible, we can work to design therapies to delay progression of the disease and maximise the length and quality of life for MND patients," he says.

His team is also working to identify the gene variations that put people at risk of developing sporadic MND, whether it is combined with lifestyle choices or exposure to environmental factors. He is hoping this work may open up other avenues to develop therapies.

"There are many ways to kill a motor neuron," says Professor Ian Blair.



GENETIC COUNSELLING

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

"Families with MND 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."

Those patients can undergo genetic diagnostic tests. Around 60 per cent of MND families have a known mutation. Early diagnosis informs clinical care and may extend life. "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.





GENOME SEQUENCING

Professor Blair’s team is using DNA samples to sequence the entire genome, the three billion letters in the genetic code of MND patients, in Australia and also as part of an international consortium that seeks to identify the genetic and environmental factors that increase the risk of developing sporadic MND.

His team includes coding experts who use high-powered computers to decipher the genomes. This allows them to compare the genomes of MND patients and contrast them with those people without MND.

They can then spot unique changes in the code that cause MND or that make people susceptible to developing the disease.

The genetic discoveries inform the Centre’s ongoing research, which seeks to understand how a motor neuron dies and to develop new therapies. When the team identifies a new genetic mutation, they can use it as a new tool to mimic the disease in the laboratory, put it into nerve cells or transfer into zebrafish to understand disease biology and test therapies that one day could translate to success in clinical trials.

Group Leader
Professor Ian Blair*

Postdoctoral Research Fellow, Team Leader
Dr Shu Yang*

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

PhD Student
Natalie Grima*
Sandrine Chan*
Sharlynn Wu*

**Pictured*





Cryptic clues to MND genes

Previously unknown shared ancestry among people with MND may offer clues to the genetics of the disease.

A set of twins with an MND gene first sparked the interest of Dr Kelly Williams, leader of the Genomics and Bioinformatics team at the Centre for MND Research.

“They had a specific genetic defect that should have caused them both to get the disease, but only one did,” she says. “My question was: what had set off one twin to get the disease and how was the other unaffected? Maybe this was the key to treatment.”

Williams’ team focuses on the computational analysis of the genetics of the disease. They first examine DNA samples from families with MND. One team member, Dr Lyndal Henden, has developed algorithms to find genetic

regions of the human genome that people with this disease share. The next step is to pinpoint the specific genetic defect in the DNA causing the disease.

The team also looks at the genetic modifiers of the disease that might not actually cause the disease but could influence when the person develops MND and how they are affected. They look for genetic modifiers in the DNA or other biological modifiers in these people’s RNA - Ribonucleic acid. This nucleic acid is present in all living cells and acts as a messenger carrying instructions from DNA to control the synthesis of proteins.

“If we can get a snapshot of the gene products

that are active in the RNA at any time using RNA, then we can compare those in large cohorts of individuals with MND,” Williams says. It might also determine if the individual presents with the disease when they’re very young or old, and if it’s a rapid or slow onset. Some people only live for two months after diagnosis, others for two decades.

“I am really passionate about developing a prognostic toolkit to help these families,” Williams says. “These people know they have the disease but they and their families have no idea how long they have left.”

MND IN FOCUS

Dr Williams has focused on discovering the genetic basis of MND for most of her 14-year academic career. She initially completed her PhD with Professor Ian Blair at the University of Sydney.

Then, after she won the competitive MNDRA Bill Gole MND Postdoctoral Fellowship, Blair recruited her to be part of his team at the nascent Centre for MND Research 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 in MND research 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 into a more senior role as leader of the Genomics and Bioinformatics team that she has established.





GENOMICS AND BIOINFORMATICS TEAM

FINDING GENETIC ANCESTORS

As well as using Australian data, the team has genetic code from international MND samples including Europe and New Zealand where they're looking for "cryptic relatedness": previously unknown, shared ancestry among MND families.

"Last year, we linked 21 Australian families genetically with MND and discovered they were actually one superfamily from a common ancestor in Scotland," Williams says. "We also found some sporadic MND

cases in the family that have no genetic history."

The results of the team's research will have significant genetic counselling implications for MND patients and their family members who visit the MND Clinic.

Her team is collaborating with machine learning experts and using artificial intelligence to analyse genetic code data to develop a tool to be ultimately used in the clinic.

*Group Leader
NHMRC Early Career Research Fellow*
Dr Kelly Williams*

Postdoctoral Research Fellow
Dr Lyndal Henden*

PhD Student
Natalie Grima*

**Pictured*





Hunt for biomarkers and environmental triggers

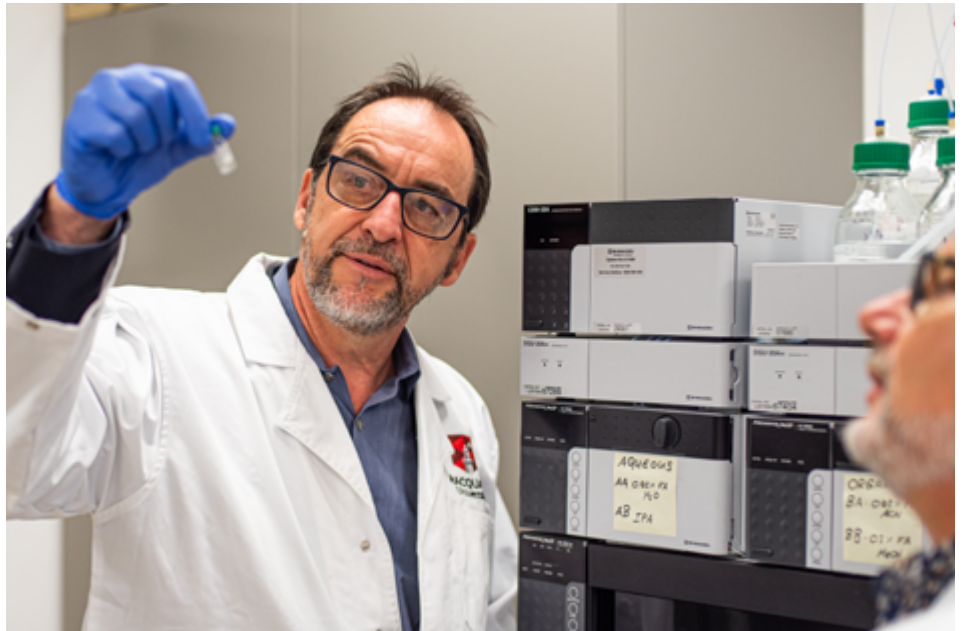
Searching for biological markers to determine the rate of progression and severity of MND, and identifying possible environmental triggers, are the two main areas of focus for Professor Gilles Guillemin's team.

Professor Gilles Guillemin oversaw the study that identified the world's first biological marker, or biomarker, for Multiple Sclerosis in 2017. 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 now 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. Dr Vanessa Tan is assessing more than 90 different molecules in the blood of these patients and comparing them to controls and analysing how they change over time.



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, Professor Dominic 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.



MICROORGANISMS

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

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



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.

In collaboration 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,” Professor Guillemin says.

The team is using satellite imagery to try to match algal blooms with the incidence of MND.

Dr Vanessa Tan was part of the international team which identified that BMAA can propagate from neuron to neuron and other brain cells, and then become dysfunctional and progressively die. This could play a role in the development of MND for people exposed to frequent algal blooms and is the hypothesis of this current project.

Tan is also developing a new fluorescent BMAA so that she can more easily study the mechanism of BMAA propagation and neurotoxicity under a microscope in real time.

Group Leader
Professor Gilles Guillemin*

Senior Clinical Lecturer
Dr Richard Schloeffel

Senior Research Fellow
Dr David Lovejoy*

Research Fellow
Dr Charlie Ahn*

Postdoctoral Research Fellow
Dr Benjamin Heng*
Dr Vanessa Tan*

Research Officer
Dr Sharron Chow*

PhD Student
Mona Dehlaghi*
Bahar Kayani*
Hamed Panahi*
Ananda Staates Pires*
Asma Oumadi*
Mahsa Vaez Zadeh*

MRes Student
Shivani Krishnamurthy*

** Pictured*





NEURODEGENERATION
TREATMENT TEAM

Pathways towards drug treatments

Researchers within the Neurodegeneration Treatment Team are testing potential treatments on zebrafish, cells and mice. The zebrafish are also helping the team better understand the degeneration of the nervous system that occurs in people with MND.

Zebrafish (*Danio rerio*) are an ideal tool to study drug treatments that may prevent or slow the development of MND. As vertebrates, they share 70 percent of their genetic code with humans and their embryos develop in days.

These tiny tropical fish can also absorb drugs added into the water they swim in, which makes it easy to dose fish that have MND with different drugs. “You can see quite quickly if it improves their movement,” says group leader, Dr Angela Laird.

Prior to joining the Centre for MND Research 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.

*“... We can actually see the glowing neurons in the living animal.”
says Dr Angela Laird.*

FLUORESCENT FISH

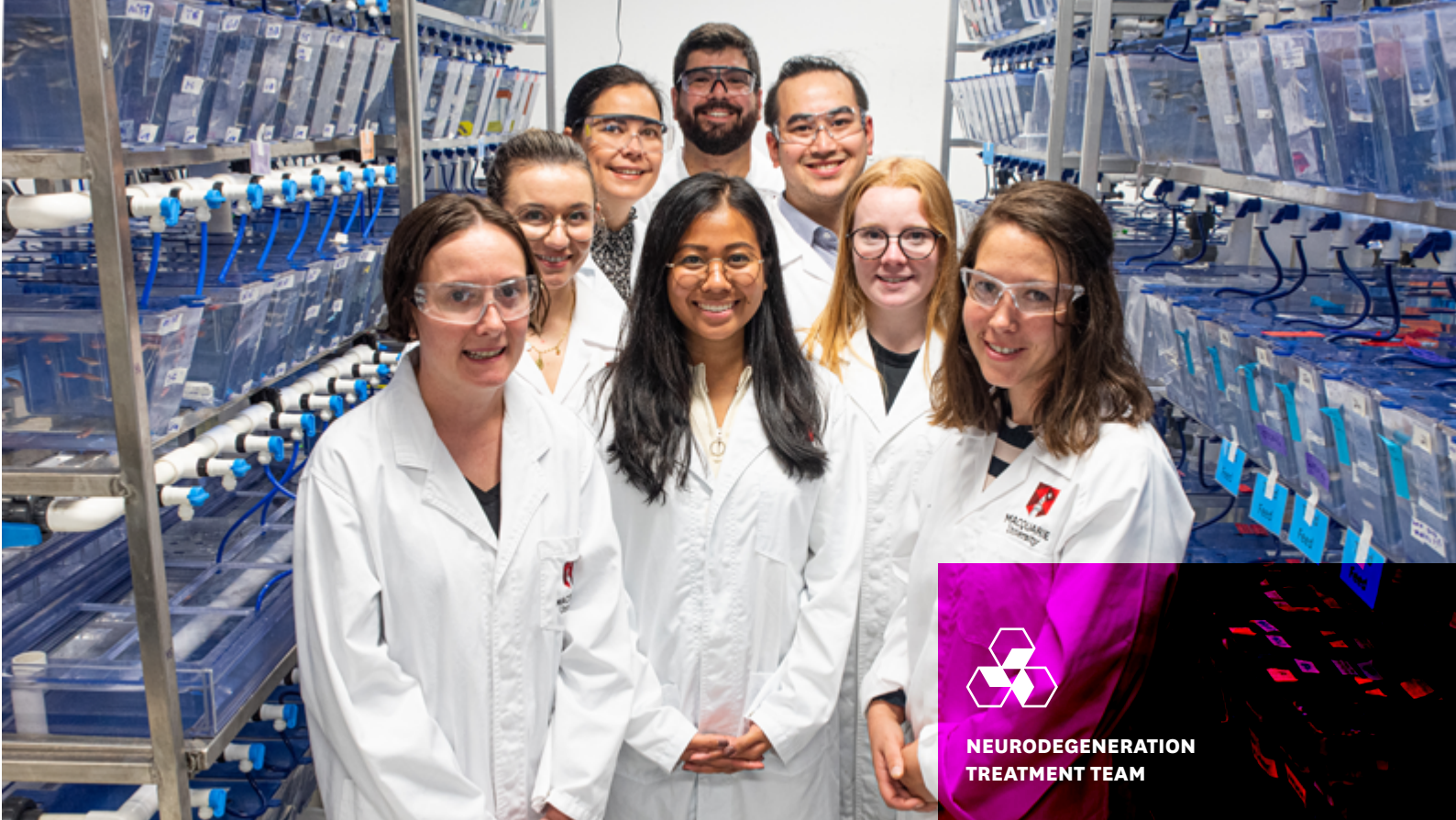
An adult female zebrafish can breed every week, producing hundreds of eggs at a time. As the eggs are fertilised and develop outside the mother’s body, they are perfect for the study of cellular processes, even in the living animal.

The embryos and juveniles of zebrafish are transparent, so Dr Laird’s team is labelling their internal neuroanatomy with fluorescent markers.

“This means we can actually see the glowing neurons in the living animal. By looking down the microscope, we can determine which drug treatments are helping the neurons within zebrafish carrying MND genes to develop more normally. This can be done more rapidly than in other animal models,” she says.

Zebrafish embryos also develop movement very early, within the first day after the egg is fertilised. “So that means for a disease like MND that affects movement, within a short timeframe we can see whether or not the mutated genes decrease their movement or whether drug treatments improve their movement,” Laird says.





**NEURODEGENERATION
TREATMENT TEAM**

Group Leader
Dr Angela Laird*

Lecturer
Dr Emily Don*

Postdoctoral Research Fellow
Dr Maxinne Watchon*
Dr Amanda Wright*

Research Assistant
Kristy Yuan
Stuart Plenderleith*
Holly Ahel*

PhD Student
Katherine Robinson*
Jack Stoddart*

MRes Student
Nicholas Kakaroubas*

** Pictured*

NOVEL DRUGS AND NATURAL PRODUCTS

The team's investigation of potential treatments for MND includes testing novel drugs that have only just been synthesised and other drugs created to treat other diseases that could be repurposed to treat MND.

Her team is also starting to test natural compounds produced from plants and marine invertebrates through a collaboration with the Griffith Institute for Drug Discovery at Griffith University.

Successes so far include discovering positive effects of treating their zebrafish models of neurodegenerative disease with a few drugs that already have approval for human use from the Therapeutic Goods Administration. These drugs remove some of the toxic

proteins that cause those diseases. Testing of these drugs on the MND zebrafish is underway.

Dr Laird's team is also collaborating with Professor Atkin's Cellular Neurobiology team to explore their potential drugs on the MND zebrafish with some positive effects already seen. Dr Laird's team has identified which of these compounds was most protective for the MND zebrafish and now Professor Atkin's team is testing these.

The next step is to test the effect of the drugs that show the most potential on other preclinical models of MND, examining whether they can improve movement and protect against neurodegeneration in those models as well.





CELLULAR
NEUROBIOLOGY TEAM

Cell biology informs drug quest

Investigating cell biology and how MND operates at a molecular level is critical to informing the design of drugs to slow its progression and even cure the disease.

“We want to know how and why motor neurons die,” says Professor Julie Atkin, leader of the Cellular Neurobiology team, who is internationally recognised for her research on cellular mechanisms leading to neurodegeneration in MND.

“So far, we’ve identified some cellular pathways that go wrong in MND and those are our biggest successes.”

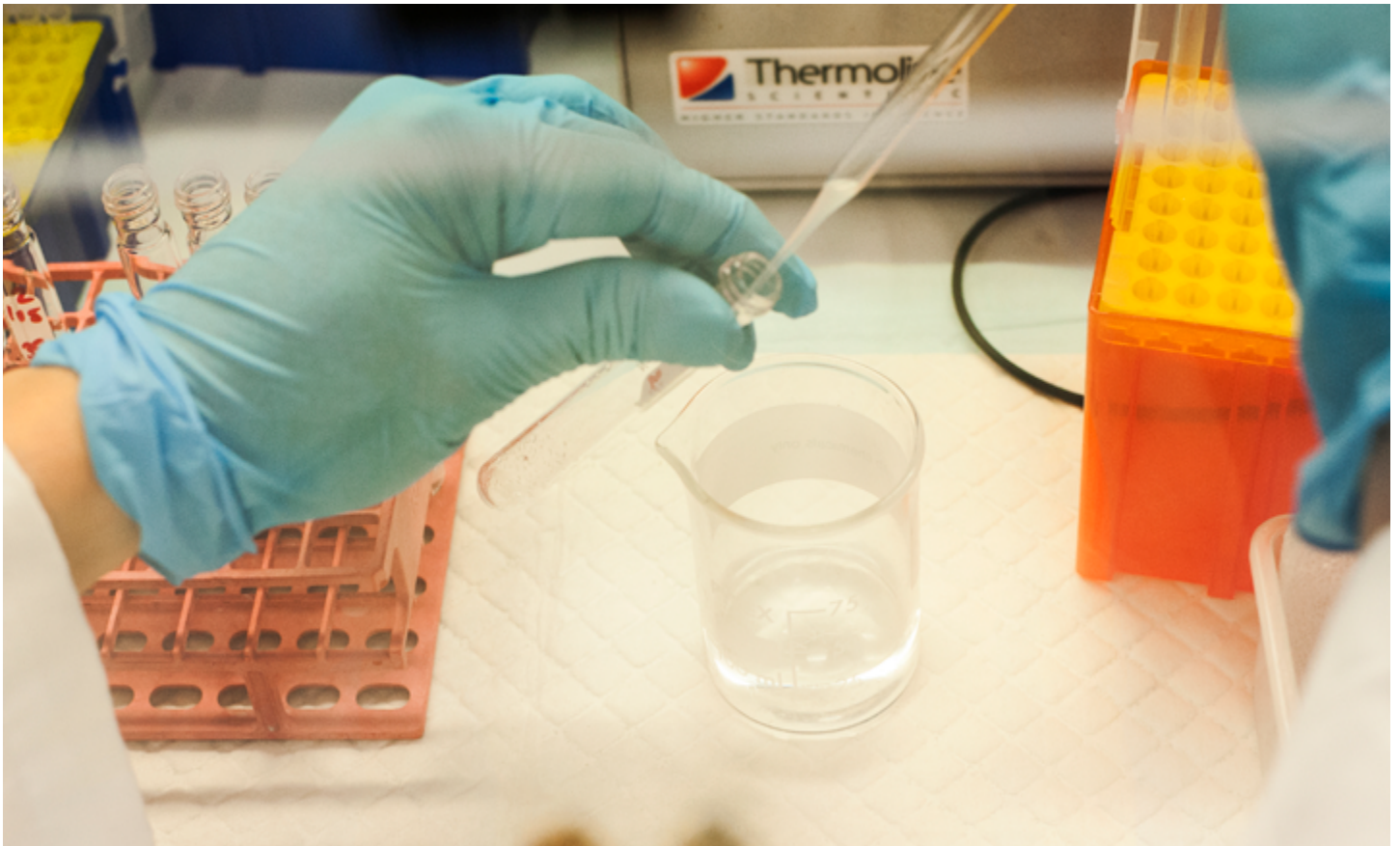
DISEASE PROCESSES THAT CAUSE MND

Her team has found that transport of proteins within the motor neuron does not function properly in MND, and this is triggered by many different genes that cause genetic forms of the disease.

Some of the team’s 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 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’s cellular investigation feeds back into their research on potential drugs. “The focus of our research is to pinpoint the first things that go wrong in MND, because then we can target drugs to prevent the disease progressing at the early stages,” says Atkin. “We’re trying to find the most upstream drug target because we believe this has the greatest probability of success.”





CELLULAR NEUROBIOLOGY TEAM

DRUG TESTING

Professor Atkin's team is using this knowledge to test three types of new drugs, initially on cells grown in the lab.

An important tool in this 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. Those drugs that prove effective in cells are then being trialled in zebrafish that develop MND, and then in transgenic models.

The team is also drawing on the expertise of chemists at La Trobe University in Melbourne and at the University of Queensland to improve the pharmacological properties of these drugs so they are more tolerable in the body.

"This is important for the drug to be effective on people, as well as stopping motor neurons from dying," says Atkin.

Hopefully, some of these drugs may eventually make it into human clinical trials."

TESTING HETEROGENEITY

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. In some people, the disease presents in the limbs, but in others, in muscles that affect swallowing. Some people survive for years after diagnosis and others only weeks.

Importantly, some motor neuron cells live longer in MND than others. For example, motor neurons innervating the ocular muscles that control eye movement don't degenerate until the very end stages of the disease, whereas motor neurons in the spinal cord fail early in the course of MND. This new project aims to determine why certain types of motor neurons are more susceptible than others.

Group Leader

Professor Julie Atkin*

Postdoctoral Research Fellow

Dr Mariana Brocardo*

Dr Cyril Jones-Jagaraj*

Dr Anna Konopka*

Dr Sonam Parakh*

Dr Sina Shadfar*

Research Officer

Dr Prachi Mehta*

** Pictured*





MULTIDISCIPLINARY
MND SERVICE AND CLINIC

Clinic at the frontline in MND battle

The Multidisciplinary MND Service and Clinic, established in 2010, is the largest integrated MND clinic in Australia, managing 200 patients at any one time.

Located right next door to Macquarie University Hospital (MUH) and linked by an overhead walkway, the Multidisciplinary MND Service and Clinic was established to serve the multiple needs of MND patients. It currently manages about 10 per cent of people in Australia with the disease.

“It aims to be a one-stop shop,” says Professor Dominic Rowe, the neurologist who leads the Clinic. “It focuses on patient-centric care and we try to anticipate clinical issues before they arise.”

Patients come in every three months for consultations with a physiotherapist, speech pathologist, dietitian, occupational therapist,

social worker, clinical nurse consultant, genetic counsellor, respiratory physician and with Rowe, depending on their stage of the disease.

Costing \$500,000 a year to run, the Clinic operates entirely on donations, which cover salaries and access to care, no matter if the patient lives in Sydney or regionally. The Clinic supports remote and rural patients by telemedicine if required. The cost to the patient to visit the clinic is minimal (approximately \$30 out of pocket), with the actual cost met by donations.

Rowe and his team also look after MND patients in MUH. The Centre uses its

charitable fund to pay for patients without private health insurance to be admitted to hospital when appropriate.

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 their MND. There are now more than 35 genes known to cause inherited MND, and families have access to in-house genetic counselling at no cost.

Another goal is to establish low-cost access to advanced IVF techniques to ultimately eradicate the genes that cause MND.



“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 TRIALS

The Clinic is the springboard for the Centre’s clinical trials. The Clinic is the lead site of a world-first trial of a novel therapy called Copper ATSM. Developed in Australia, Cu-ATSM aims to rebalance the metal deposition abnormalities that occur in brains of MND patients, resulting in increased iron and reduced copper in neural tissue. Phase 2 of this trial has now concluded and the results are being analysed, with release later in 2021.

The Lighthouse 2 Trial, an international Phase 3 Randomised double blind trial of the antiretroviral therapy Triumeq is due to start in Q4 of 2021, after many delays because of COVID in Europe. This trial will determine whether antiretroviral therapy is able to slow the progression of sporadic MND.

Macquarie University is to trial a novel therapy 3K3A-APC in MND, an intravenous therapy that has both anti-inflammatory and neuro-protective effects. This novel therapy will be trialled in a small cohort of patients with ALS, beginning in October 2021. Completely funded from donations by the Firies Climb for MND, the study uses several novel mechanisms to measure drug effect in the brain of patients with MND.

Three further trials are to start in Q4 of 2021. Macquarie is the only site in Australia in the Atlas study, a trial of a novel gene therapy in patients carrying

a mutation in SOD1 as the cause of MND. The WAVE study will use a gene therapy in an attempt to slow the progression of MND in patients with an expansion in the gene C9ORF72. Finally, a Phase 1 trial of a therapy termed Monepantel, an mTOR inhibitor is due to start in January, funded by FightMND.



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

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

Corinna Pan*

MND advisor from MND NSW

Lucy Hobbs*

** Pictured*



NEURO-IMPROVE
GROUP

Proteins unlock pathways to therapy

Professor Roger Chung leads the NEURO - IMPROVE Group at the Centre for MND Research. IMPROVE stands for Imaging Proteomics Therapeutic Delivery.

POTENTIAL GENE THERAPY

After Professor Ian Blair's group discovered a new gene that causes MND in 2015, Professor Roger Chung's team embarked on research to understand how that gene causes motor neuron degeneration. The team's research uncovered the role of the protein encoded by this gene as a key component of



“The early phases of this research were fully funded through donations for MND research. Without this support this new area of research would not have been possible,” Chung says.

the intracellular pathway responsible for clearance of damaged/accumulated proteins.

“Importantly, we showed that the disease variant caused abnormal accumulation of proteins inside motor neurons, which is one of the characteristic hallmark pathologies of MND,” Chung says.

To his team's surprise, they found that overexpressing a therapeutic variant of the gene could prevent disease pathology, and these discoveries have led us to the development of a potential gene therapy for MND.

These discoveries have been patented and his team is conducting pre-clinical testing of the potential gene therapy in collaboration with researchers from Children's Medical Research Institute, University of Queensland and Flinders University. These research projects are supported by research funding from the MNDRIA, National Foundation for Medical Research & Innovation and FightMND.

DISCOVERING NEW DISEASE BIOMARKERS

Chung's team is identifying new disease biomarkers using unbiased molecular technologies that may allow earlier disease

diagnosis or measures of disease progression and severity.

“We are looking to identify precisely how things go wrong inside motor neurons in MND, which will give us new ideas for how we can protect the neurons and find out whether there are biomarkers in the blood that can inform us of disease onset or progression,” Chung says.

To do this, the team uses two different experimental approaches. The first uses an antibody to specifically bind to MND disease proteins, followed by an enzymatic reaction that ‘sprays’ a label onto surrounding proteins. This allows the researchers to subsequently extract and identify the full composition of the toxic protein aggregates in MND.

The team then works backwards to understand how these aggregates form and which of their components could be targeted to prevent their formation and/or toxicity.

In the second approach, the team uses technologies to identify protein-fingerprints in blood samples that are unique to MND patients. They are working with collaborators at Griffith University and Sydney University supported by the MNDRIA.

ACROSS THE BLOOD-BRAIN BARRIER

Associate Professor Bingyang Shi leads the Brain Drug Delivery group which is developing ‘smart’ nanoparticle-based solutions to carry drugs into the brain and target specific cells.

A significant hurdle for any therapeutic treatment for neurodegenerative diseases is how to deliver drugs to the brain or spinal cord. They are covered with a protective barrier called the blood-brain barrier, a layer of cells specifically designed to keep

the brain separate from the rest of the body.

A second challenge once drugs cross this barrier is how they can specifically target diseased cells and not healthy ones. This group is supported by an NHMRC Investigator grant.



NEURO-IMPROVE GROUP MEMBERS

PRIOR NEURODEGENERATIVE RESEARCH

Professor Chung has had a longstanding interest in MND research, being the inaugural recipient of the Bill Gole Fellowship awarded by MNDRIA. Before he came to the Centre for MND Research, he led a team at the University of Tasmania that focused on metallothioneins (MTs), a highly unusual family of metal binding proteins whose precise physiological functions remain unclear. Chung's team was the global leader identifying precise links between MTs protein structure, its unique biochemical properties and biological functions.

Some of the major achievements included the discovery that extracellular MTs have neurotrophic activities and play an important role in astrocyte neuron responses to injury. This revealed that MTs (and MT-based peptides) have potential neuroprotective and neuroregenerative activities and could have therapeutic potential against amyloid toxicity in Alzheimer's disease. These discoveries were patented and licensed to a biotech company for further therapeutic and commercial development.

Group Leader
Professor Roger Chung*

*Senior Lecturer,
Group Leader*
Dr Albert Lee*

*Senior Research Fellow,
Group Leader*
Dr Marco Morsch*

*NHMRC Investigator
Fellow, Team Leader*
**Associate Professor
Bingyang Shi**

MQ Research Fellow
Stephanie Rayner*
Dr Anne Zhou

*Postdoctoral Research
Fellow*
Dr Luan Luu*
Dr Jia Li *

Dr Cindy Maurel*
Dr Alison Hogan
Dr Nima Sayyadi*

Research Assistant
Flora Cheng
Guoying Wang*
Tyler Chapman*
Rowan Radford*
Stephen Cull*

PhD Student
Afshin Babazadeh*
Jennilee Davidson*
Natalie Schrerer*
Hannah Suddull*
Andres Vidal-Itriago
Paulina Szwaja
Yang Liu

** Pictured*





A live-stream into the brain

Zebrafish are transparent when they're young, so researchers genetically modify the fish to label their motor neurons and human MND proteins with fluorescent markers.

Dr Marco Morsch's Neuroimaging team works with zebrafish to visualise how MND-specific clumps form within nerve cells and how these circulate throughout the nervous system. These fish provide researchers a unique opportunity to observe how MND develops within nerve cells and how they can potentially target this disease therapeutically.

The first stream of his team's research is to gain basic understanding of what happens to the disease proteins that clump together in neurons. The researchers then use innovative strategies to kill these neurons and follow up what happens - such as whether they can spread to the neighbouring cell.

THE GARBAGE COLLECTORS

Morsch's team has identified a 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 - they are the garbage collectors of the central nervous system, Morsch says.

"When we experimentally interfered with this 'housekeeping service', we discovered that the aggregates can disperse in unprecedented ways. Once we understand these pathways better, we hope to identify novel opportunities to delay disease progression," he says. "We've discovered that the disease spreads further when microglia can't do their job."

His team also looks at atrophy in protein clumps or aggregates - how they are modified normally and how they change when they're

affected by MND. His team can use advanced microscope techniques to see how they change their behaviour.

Finally, they're also 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.

Zebrafish provide researchers a fast track because they develop a central nervous system in a couple of days and it's possible to test compounds quickly and assess how they affect critical mechanisms.

"We spend a lot of time in dark rooms with big microscopes, to visualise these tiny cells but we have a lot of fun and really enjoy doing it," he adds.

"It's mind blowing," says Morsch. "I remember the first time when I saw the fluorescent labels in a fish and cells moving around within a living organism and I thought it was fascinating. We can 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."





NEUROIMAGING AND DEGENERATION TEAM GROUP MEMBERS

DIFFERENT NEURON FOCUS

Morsch completed his PhD at the University of Bonn in Germany in 2009 and then came to Australia to the University of Sydney to do postdoctoral research on neurons in the central nervous system.

The Centre for MND Research at Macquarie then 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.

Initially, for his first four years at the Centre, Morsch worked as a researcher within Professor Roger Chung's Neuro-IMPROVE group. By 2018, it was a natural progression that Morsch's team would split off into a discreet group - particularly after receiving external recognition from grant funding agencies and making seminal contributions to his research field.

In 2018, Morsch was awarded the Outstanding mid-career researcher prize by MND Research Institute of Australia.

Group Leader
Dr Marco Morsch*

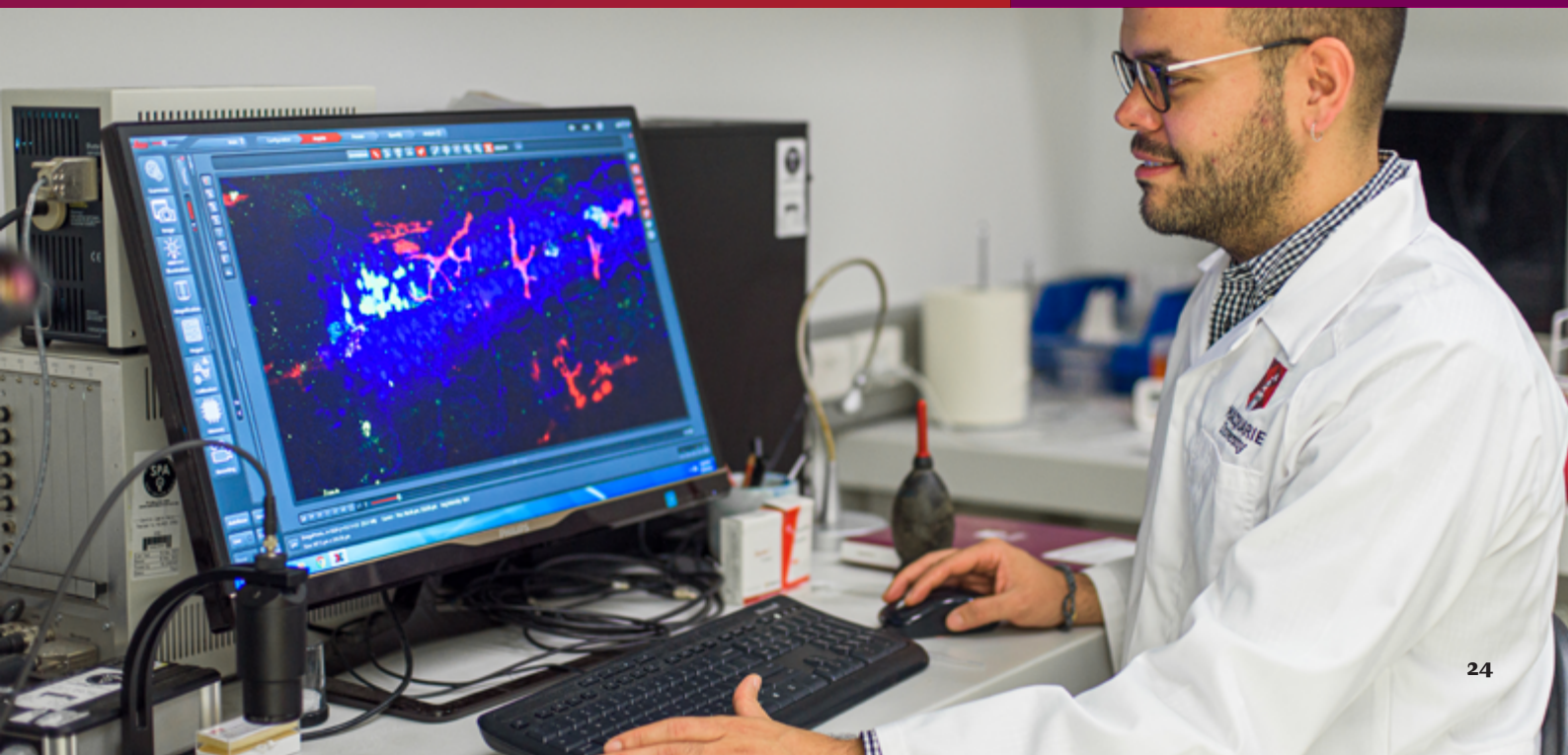
Lecturer
Dr Emily Don

Postdoctoral Research Fellow
Dr Alison Hogan*
Dr Luan Luu*
Dr Cindy Maurel*

Research Assistant
Tyler Chapman*
Stephen Cull*

PhD Student
Natalie Scherer*
Andres Vidal-Itriago*

** Pictured*





Clues to zero-in on MND's cause

By focussing on proteins and how they behave with each other, researchers are inching towards discovering which proteins cause motor neuron defects

Dr Albert Lee leads the NeuroProteomics Research Team at the Centre for MND Research. Proteomics is the study of how proteins function and interact with each other, such as creating 3-D structures or other shapes to perform their functions.

Lee and his team are researching why and how MND-specific protein clusters form and alter normal protein pathways within cells. They have identified some key proteins involved in the initial stages of this MND-specific protein "aggregation" or clumping.

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

To do a lot of their analysis, the researchers use a mass spectrometer that measures molecules, such as proteins made by cells with gene mutations that cause MND. This procedure enables the researchers to capture a snapshot of the cellular or disease state.

"We are trying to determine how gene mutations affect proteins and how these protein defects affect the motor neurons that ultimately cause MND," Lee says.

"Compared to other areas like cancer, proteomics in MND is still in its infancy and has not been studied much globally."

TAKING THE WEIGHT

The mass spectrometer weighs the mass of all the molecules at rapid speed and then Lee analyses the results manually. He also uses a process called 'unbiased proteomics', to see how the proteins behave in different MND models.

"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 establishes MND models so other researchers can test therapies in models such as zebrafish. Lee and his team have filed a portfolio of patents that describe these therapeutic

concepts and are in the process of preclinical therapeutic evaluations.

Lee also develops and drives research projects within the proteomics program as part of the NHMRC Dementia Teams Grant focused on MND, Frontotemporal Degeneration (FTD) and proteostasis dysfunction. He oversees several students' research and teaches.

"My passion is educating, supervising and inspiring students to drive change and assist their own personal growth. Every student has their own valuable life experiences and my goal is to adapt my techniques to ensure each student achieves a better understanding of scientific and medical research to achieve positive outcomes," he says.





**NEUROPROTEOMICS
TEAM MEMBERS**

Group Leader
Dr Albert Lee*

Postdoctoral Research Fellow
Dr Stephanie Rayner*

Research Assistant
Tyler Chapman*
Flora Cheng*

PhD Student
Jennilee Davision*

Hannah Suddull*

** Pictured*

ROAD TO MND

Initially, Lee's group at the Centre was part of the Neuro-IMPROVE group led by Professor Roger Chung. But their research grew exponentially and by natural progression, Lee formed his own independent proteomics group in late 2019. He now works with a staff of six researchers.

Lee has worked at the Centre for MND Research for seven years. After finishing his PhD at Macquarie University, he worked at the New York University School

of Medicine in the US as a proteomics scientific officer. He then did his three-year postdoctoral research fellowship at the Johns Hopkins University, School of Medicine in Baltimore.

When Professor Chung offered him a role back at Macquarie, he returned to Australia in 2014. Lee's mandate 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 MQU Centre for MND Research and clinic.



Kaitlin, Jessica and Susan

In 2010, Kaitlin and Jessica Ellis' uncle lost his battle with motor neuron disease. Five years later, their mother, Susan, started showing similar symptoms. Her foot began dropping and she frequently fell over. Doctors thought she had arthritis.

Kaitlin and Jessica's worst fears were realised when their 57-year-old mother tested positive for MND. They immediately gave up their jobs and study to jointly care for Susan full-time at home for two-and-a-half years. Susan died in 2017.

"It was so hard to watch our mum, knowing she had a terminal illness with no cure. The person we loved the most just declined more and more every day," says Kaitlin, who was 21 at the time and working as a nurse. "Mum was everything to us. We looked after her 24/7 and

faced many challenges, but it brought us all much closer together." Jessica, 24 at the time, was a legal secretary.

Susan's doctors at Liverpool Hospital suggested her daughters undergo genetic testing. They discovered they both carried the gene that caused MND. "Getting genetic testing is a very personal choice and everyone reacts differently," Kaitlin says. "I'd seen how my uncle and Mum had suffered and I didn't want anyone else in my family to suffer like that, let alone myself."

Jessica and Kaitlin chose to get genetic testing so that in future, they can go through IVF and hopefully have a child who isn't a carrier. The sisters now give annual blood samples to the Neurodegenerative Disease Biobank.

"In retrospect, I wish I had waited until after Mum had passed away to get tested," Kaitlin says. "When I told her, it absolutely broke her. She cried and cried. It was devastating for all of us."



The sisters have set up a support group called MND Genies, for people like themselves who have an MND genetic mutation but haven't yet developed the disease.

Cobie, Luke and Mick

Luke Smith's father, Mick died from MND in 2017. He'd been diagnosed about 15 years earlier. Luke's two siblings had genetic testing and had no trace of the genes known to cause MND. When Luke took the test, he discovered he was a carrier of familial MND.

"It took a long time to sink in and I felt pretty horrible," says Luke. "But I came good after about six months." Newly married to Cobie, and the couple, both 24 years old at the time, decided to use IVF to conceive.

"It was pretty clear to us once I discovered I was gene-positive," Luke says. "We'd watched my father deteriorate and suffer. We knew we wanted to have kids but we didn't want them to carry this gene, so doing IVF was an easy decision for us. The technology's there, so why not use it?"

Luke and Cobie started the IVF process in March 2012. Cobie says it was very difficult and stressful. "I found it hard mentally and I

wouldn't wish it on my worst enemy," she says. "But it has given us peace of mind down the track."

The couple was fortunate to have financial backing but would have loved to have more emotional support. "We were the first couple with hereditary MND that our fertility doctor had dealt with," Cobie says. "I felt totally isolated. There was no one else in my life who could understand what I was going through. We were walking into the unknown."

Their first daughter was born in December 2013 and their second in 2017. Cobie says she'd love to talk to other couples to give them the support they themselves never had.

GENETIC COUNSELLING SERVICE

Rosie Fell is one of the genetic counsellors at the Multidisciplinary MND Service and Clinic. She counsels patients and relatives of patients about familial MND. Individuals may be referred to her by Professor Dominic Rowe if he suspects they have inherited MND because multiple members of their family have had the disease. Some individuals request a referral about themselves, as they are concerned about a personal or familial risk of MND.

Fell gathers family history information from both maternal and paternal sides. If relevant, she will then offer genetic testing. "Our role is to give our patients all the information in a way that they can understand, so they can make an informed decision about their health and decide what to do next," Fell says. "If their MND is genetic, then that may have implications for other family members."



Luke provides biological samples to the Neurodegenerative Diseases Biobank. Mick was a patient of Professor Dominic Rowe at the Multidisciplinary MND Service and Clinic.

Riding the wave of MND

Ros and Brian have had a 40-year relationship, started a company, raised a son and embraced an outdoor lifestyle. Now their challenge is living with Brian's diagnosis of sporadic MND.

Born in the UK, Ros came to Sydney in her late 20s and met Brian, who describes himself as "seventh-generation Australian from convict stock". Brian had just returned from travelling and working in Asia and Europe.

Growing up in Lismore on the North Coast of NSW, longboarding was his first and lasting passion. In the 1980s, Brian and his business partner caught another wave - the burgeoning technology industry — and set up an IT company.

Ros and Brian raised a son and had a decades-long adventurous outdoor lifestyle; surfing, skiing, cycling and hiking, taking every opportunity they could to travel in Australia and internationally..



"We want as many people as possible with MND to benefit from the ground-breaking research and specialist care offered at Macquarie," Ros says.



'VISIONARY PROJECT'

In May 2020, when Brian was 70 and enjoying an active retirement, he was diagnosed with sporadic MND. "It was a bit of a thunderbolt," says Ros. Brian's GP referred him immediately to Professor Dominic Rowe at the Interdisciplinary MND Service and Clinic at the Centre for MND Research.

"Our biggest concern right after the diagnosis was: 'will we get the support we need?' and we're so lucky that Dom's clinic has given us such multifaceted and tailored care," says Ros. "We call it MND speed dating as the neurologist, speech therapist, dietician and others all come in to help us."

The couple recently had a tour of the Centre. "We found it very uplifting, hearing how people had come from all over the world to bring their research expertise together to create this centre," Ros says. "It's a really visionary project that's touching thousands of people's lives."

Brian is very grateful that he lived a full and happy life before he developed the disease and the expert care he's received since. For this reason, to support more research and the work at the clinic, Ros and Brian have given a generous donation to the Centre.

For the moment, Ros and Brian are still enjoying time together outdoors, such as walking along Balmoral Beach. "Brian still has his dry sense of humour and we have fun," Ros says.

Supporting research for a cure after a fortunate life

Half a century-long marriage, a full life and an active retirement were disrupted when Rob Parsonage developed MND in 2019.



Weeks before his death at the age of 75 in February 2020, Rob decided to make a substantial annual contribution to the Centre for MND Research. “He was always searching for answers to everything and he was very supportive of research to find a cure for MND,” she says.

TIRELESS AND FORTUNATE

Rob had grown up in Hornsby in northern Sydney in a family of fourth generation butchers. His family established the first KFC franchise in Australia, which Rob then took over and became an energetic serial entrepreneur.

“For the first ten years of our marriage, Rob would be up at three am, going to the abattoir in Homebush to buy the meat for the butcher shop, come home and have a sleep until about 10 and then up again, working at one of the chicken shops and stay there until about 11 at night, seven days a week,” Sandy says.

Simultaneously, he created the Black Stump chain of steakhouses which he ran for 35 years.

The family also had a sheep farm, a travel business and later bred racehorses. He left behind three sons, a daughter and nine grandchildren. “Rob always said he was grateful that he’d led such a fortunate life,” she says.

Half a century-long marriage, a full life and an active retirement were disrupted when Rob Parsonage developed MND in 2019.

After a working life running a slew of successful businesses, Rob Parsonage immersed himself in an active retirement kayaking, going to the gym everyday and playing golf regularly.

“Then, all of a sudden he started noticing that he was having trouble tying ties and doing up buttons and even the mouse on the computer became difficult to use,” says Sandy, his wife of 50-years. “He thought maybe he’d had a minor stroke and he also went to see a hand specialist.”

It was only after a brain scan that the devastating truth was revealed. Professor Dominic Rowe at the Centre for MND Research confirmed that Rob had advanced sporadic MND.

“The worst thing was that Rob was just plain terrified,” says Sandy. “He didn’t know how

much time he had left and felt he had so many finances to tidy up. He had an incredible strength of personality that never left him. He also kept up his dark humour right until the end.”



Giving for future generations

A few years ago, Mike Chisholm's mother died of MND in New Zealand. Since then, he's become a regular financial donor to the Centre for MND Research because he's impressed by the passion and commitment of the researchers and clinicians.

When Beth Chisholm died of MND in New Zealand in 2011, her son, Mike, who was living in Sydney and CEO of Crestone Wealth Management, took a keen interest in investigating MND research around the world. He soon found the Centre for MND Research at Macquarie University.

"I took the initiative to go out to the Centre and see what they were doing," Mike says. "I found a group of extremely talented but equally passionate people. For them, it is far more than just a job. They are fully invested in what they do and that's why they've had such incredible results."

Mike was really amazed by the Centre's multidisciplinary approach, providing tailored care for MND patients and their families,

while researchers also conduct ground-breaking research and world-first clinical trials. "I am extraordinarily impressed with what they've created from nothing."

In 2016, Mike became an annual donor to the Centre and also actively participates in the Centre's gala and fundraising events. He encourages other people who can, to donate.

"If people are lucky enough to have either well-paying jobs or have inherited reasonable sums of money or gained it through some other event, then I have a view they have a responsibility to support the community we live in," Mike says.



Giving to an organisation such as the Centre for MND Research helps develop treatments and cures for future generations, he says. "I also get a huge satisfaction, a sense of pride, when I hear what the team at the Centre has been able to achieve, their discoveries and ongoing research. They're solving really challenging problems and are going to have a huge impact on a large number of lives and families across Australia and the world."

Alumni urged to donate

Alumnus David Bussman gives back to his Alma Mater and encourages others to give to the Centre that relies on private donors and research grants.



After retiring from a career as a Chartered Accountant, David Bussman decided to pursue his passion in Egyptology and enrolled in a Master of Arts at Macquarie in 1996. "The promise of a study trip to Egypt for four weeks which included inspecting Macquarie digs added to the attraction," he says.

David continued his connection with Macquarie, and with his wife Patricia, decided to invest in future generations by leaving the University a bequest in their will. They chose the Centre for MND Research after a lab tour.

"The researchers had impressive zeal and optimism, and realised they may well be 'in the trenches' for a long haul before they can win the fight against MND," says David. He believes in 'leading from the front' and hopes other alumni and employees will follow suit.



Country town rallies

Residents of Bathurst, three hours' drive west of Sydney and best-known for its annual 1000km supercar race, showed their generous spirit when a local developed MND.

Tony Campbell, a businessman in Bathurst, was diagnosed with MND in March 2018. His decline was swift, says his partner Janine Graham. And when the couple visited the Centre for MND Research and attending Professor Dominic Rowe's Multidisciplinary MND Service and Clinic, they decided to raise funds to support its work.

"Seeing all the younger people who'd been diagnosed with MND made us really want to do something," Janine says. "It's too late for Tony, but maybe in the next few years researchers will find what causes this disease or find a cure."

Janine began organising fundraising efforts and in April 2019, local townspeople in

Bathurst showed their overwhelming support, donating more than \$50,000.

"Country towns are very good at rallying around one of their own who is going through difficult times," Janine says. "It was really fun for Tony and I to organise the night and it gave us something different to focus on a while."

Events

FIRIES CLIMB FOR MND

When NSW firefighter Matt Pridham's best mate Adam Regal was diagnosed with MND in 2013 at age 32, the news could not have been more devastating.

Willing to stand up and take action, Matt approached Macquarie University with an idea to raise \$50,000 to support the Macquarie University Centre for Motor Neuron Disease Research. His idea — to invite firefighters to climb Sydney Tower Eye in their full 20kg firefighting uniform.

In the last five years, Firies Climb for MND has raised more than \$3 million, enabling the MND research centre to progress its research by leaps and bounds.



NOT A NORMAL YEAR

In a “normal” year, the Firies climb the 1,504 steps of Sydney Tower Eye but 2020 was anything but normal. The Firies adapted and challenged everyone to climb 1,504 steps, or cycle 15.04km, or walk for 150.4 minutes or participate in any physical challenge that related to the number 1,504 - then challenge three other people to do it. These pictures show all the innovative activities people did to raise money for MND.



ANNUAL CONFERENCE

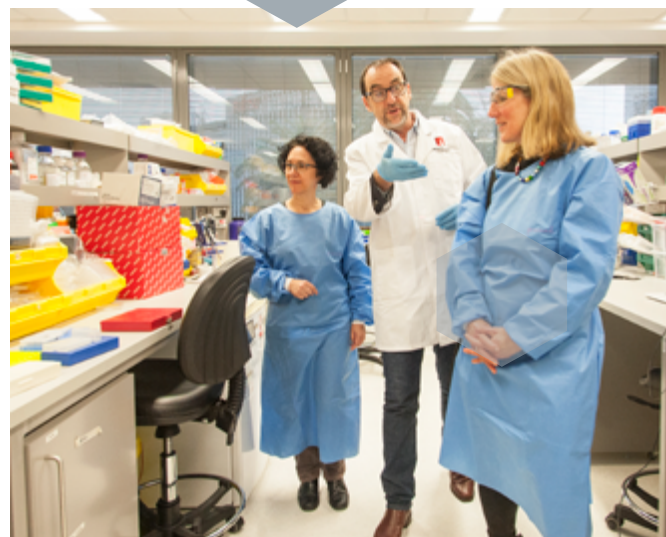
The Centre hosts the annual Macquarie Neurodegeneration Meeting, a national conference attended by more than 200 researchers and is now in its fourth year. The conference showcases the latest research on MND, frontotemporal dementia, Alzheimer's, Parkinson's disease and other neurodegenerative disorders.

It also provides an opportunity for Australian neuroscientists to network and collaborate on further research. In 2020, the conference went virtual, attracting prestigious international speakers and reaching a far wider audience. The 2021 conference will again be a webinar with a great lineup of world-recognised leaders in their field.



LAB AND CLINIC TOUR

Experience first-hand what keeps researchers and clinicians busy at the Centre for MND Research and the Multidisciplinary MND Service and Clinic. Visitors receive a guided tour of the Clinic, where more than 10 per cent of Australia's MND patients are cared for by Professor Dominic Rowe and his team, and where two Australian-first clinical trials are in progress. Then go behind the scenes into the laboratories and meet the outstanding research teams tackling MND, from diagnosis to treatment, in their quest for a cure.



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 Guillemain 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.guillemain@mq.edu.au



DR ANGELA LAIRD
Centre Executive Member and Group Leader

Dr 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



DR 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

DR KELLY WILLIAMS

Centre Executive Member and Group Leader

Dr 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

DR MARCO MORSCH

Centre Executive Member and Group Leader

Dr 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.

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.

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

DIVERSITY

1 | 1

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

17 | 8

We have seventeen female research fellows and 8 male research fellows.

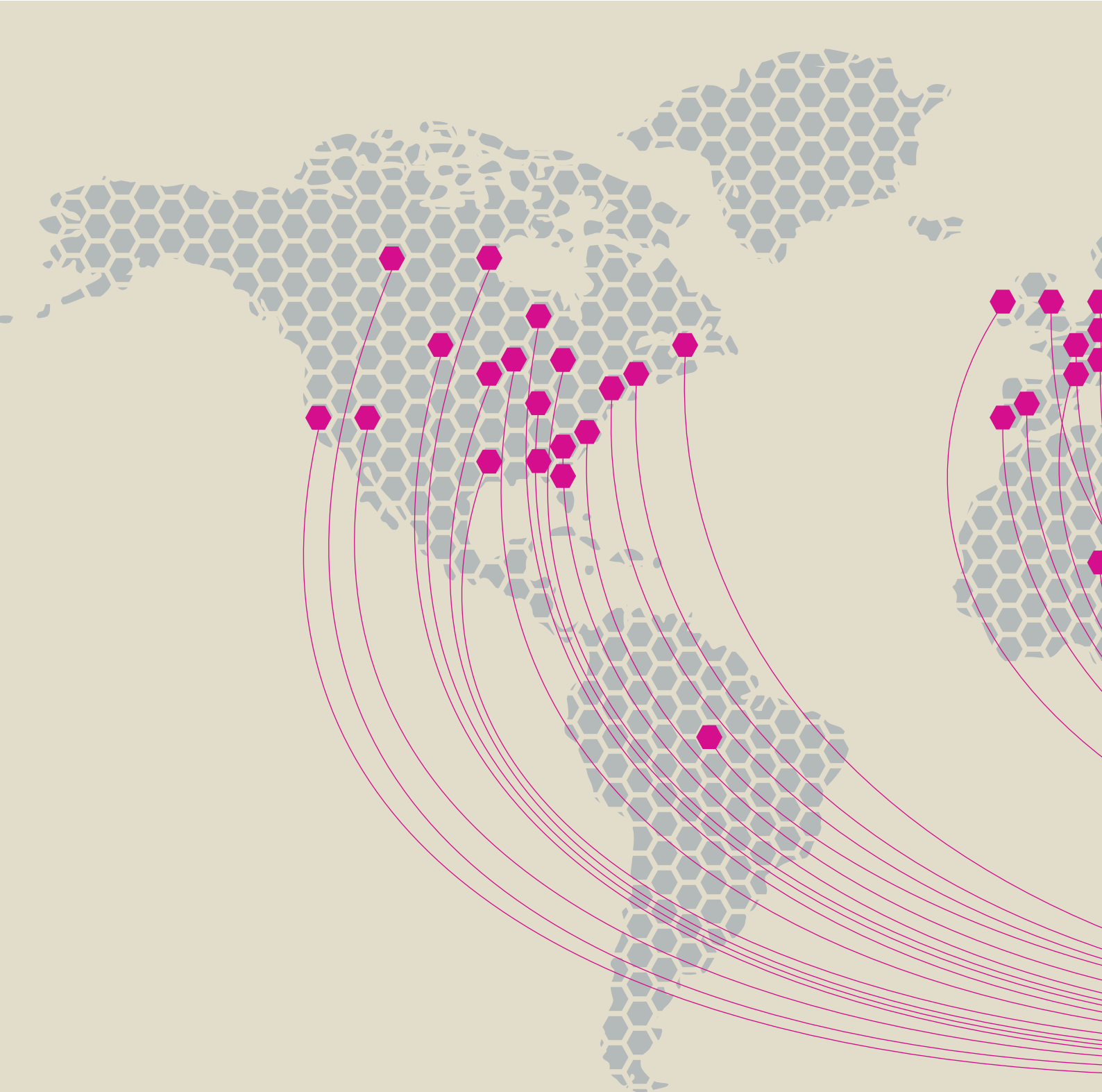
3 : 8

Our current female to male Group Leader ratio is 3:8.

60%

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

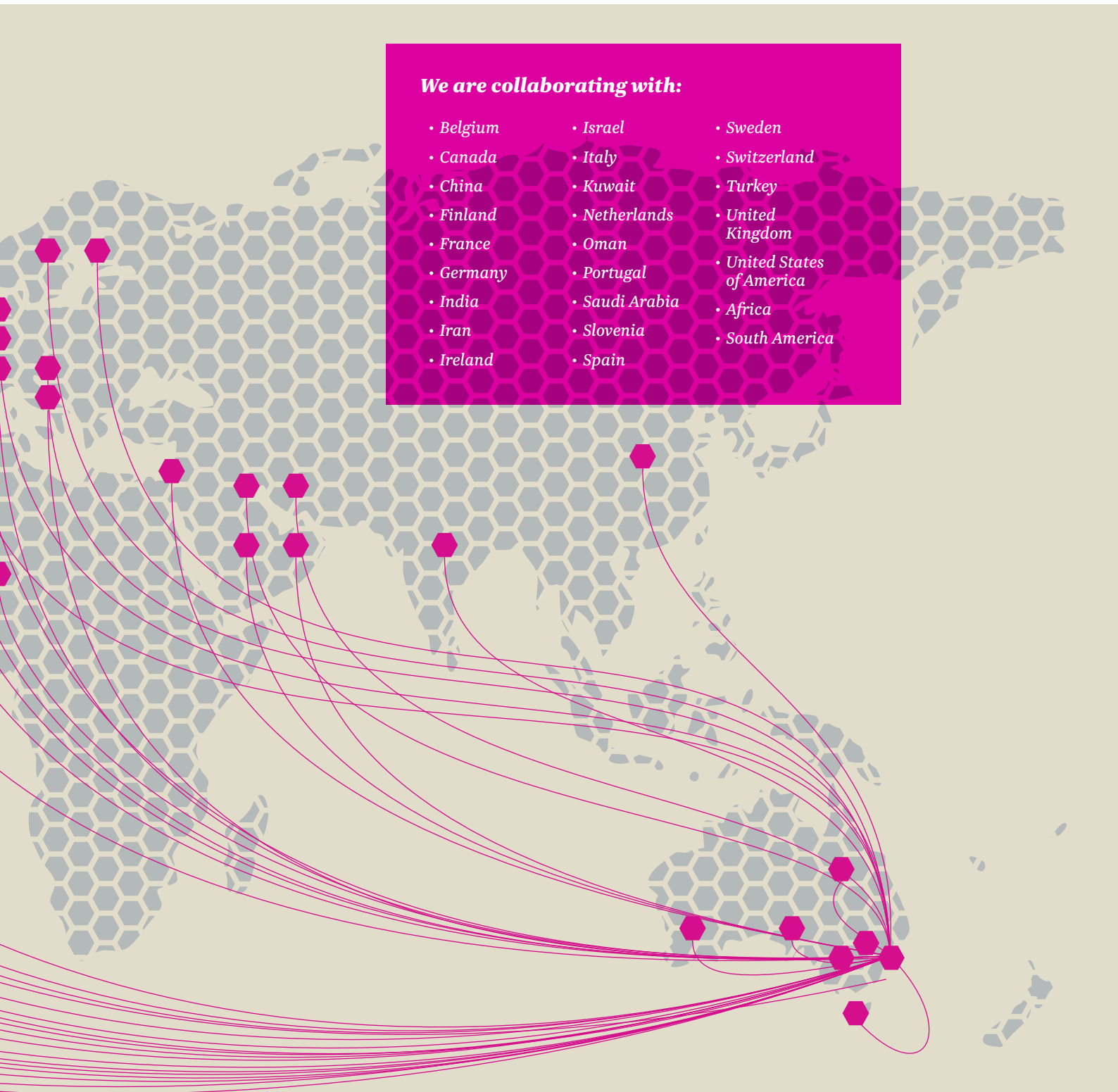
Global institutional collaborators



The Centre for MND Research has collaborated with 455 research institutions from all over the world.

We are collaborating with:

- Belgium
- Canada
- China
- Finland
- France
- Germany
- India
- Iran
- Ireland
- Israel
- Italy
- Kuwait
- Netherlands
- Oman
- Portugal
- Saudi Arabia
- Slovenia
- Spain
- Sweden
- Switzerland
- Turkey
- United Kingdom
- United States of America
- Africa
- South America



Community funds are vital for future work

Fundraising and community support are essential to ensuring the Centre for MND Research and the Multidisciplinary Service and Clinic can continue to improve the outcome of people living with MND.

We are so grateful to the thousands of people, organisations, communities and foundations that continue to support our work.

Since 2013, the Centre, Service and Clinic have received almost \$9 million in philanthropic support from our community of donors. It 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 are 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 uncover 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 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

- early and mid-career fellowships – 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 Centre for MND Research 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.



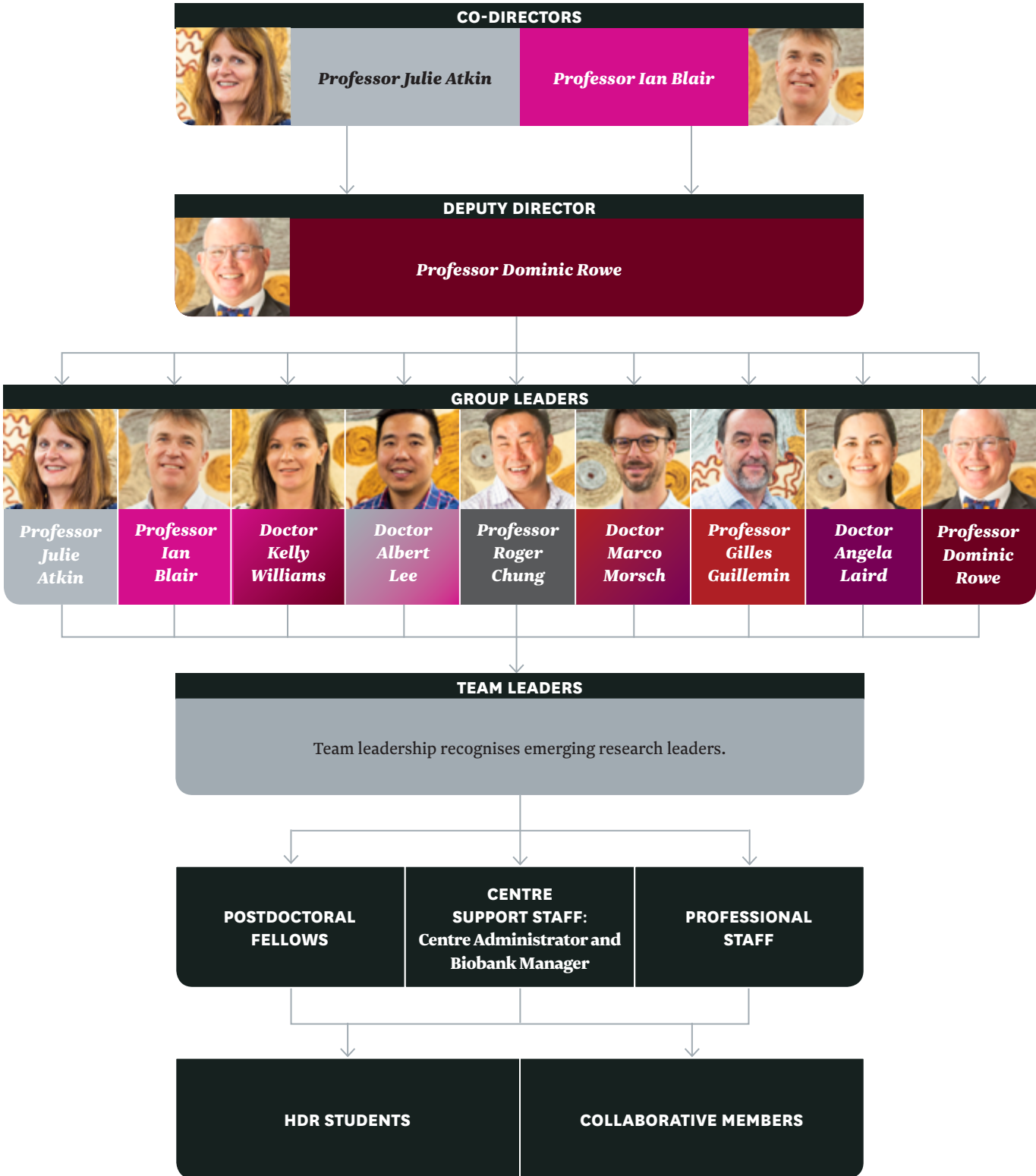
Publication highlights

08/2020 - 08/2021

- **Advances in nanotechnology-based strategies for the treatments of amyotrophic lateral sclerosis.**
Wang, G. Y.; Rayner, S. L.; Chung, R.; Shi, B. Y.; Liang, X. J. In: *Materials Today Bio*, Vol. 6, 100055, 04.05.2020, p. 1-18.
- **ALS/FTD-causing mutation in cyclin F causes the dysregulation of SFPQ.**
Rayner, Stephanie L.; Cheng, Flora; Hogan, Alison L.; Grima, Natalie; Yang, Shu; Ke, Yazhi D.; Au, Carol G.; Morsch, Marco; De Luca, Alana; Davidson, Jennilee M.; Molloy, Mark P.; Shi, Bingyang; Ittner, Lars M.; Blair, Ian; Chung, Roger S.; Lee, Albert. In: *Human Molecular Genetics*, 17.03.2021.
- **Amyotrophic lateral sclerosis-linked UBQLN2 mutants inhibit endoplasmic reticulum to Golgi transport, leading to Golgi fragmentation and ER stress.**
Halloran, Mark; Ragagnin, Audrey M. G.; Vidal, Marta; Parakh, Sonam; Yang, Shu; Heng, Benjamin; Grima, Natalie; Shahheydari, Hamideh; Soo, Kai-Ying; Blair, Ian; Guillemin, Gilles J.; Sundaramoorthy, Vinod; Atkin, Julie D. In: *Cellular and Molecular Life Sciences*, Vol. 77, No. 19, 10.2020, p. 3859-3873.
- **CYLD is a causative gene for frontotemporal dementia - amyotrophic lateral sclerosis.**
Dobson-Stone, Carol; Hallupp, Marianne; Shahheydari, Hamideh; Ragagnin, Audrey M. G.; Chatterton, Zac; Carew-Jones, Francine; Shepherd, Claire E.; Stefen, Holly; Paric, Esmeralda; Fath, Thomas; Thompson, Elizabeth M.; Blumbergs, Peter; Short, Cathy L.; Field, Colin D.; Panegyres, Peter K.; Hecker, Jane; Nicholson, Garth; Shaw, Alex D.; Fullerton, Janice M.; Luty, Agnes A.; Schofield, Peter R.; Brooks, William S.; Rajan, Neil; Bennett, Mark F.; Bahlo, Melanie; Shankaracharya; Landers, John E.; Piguat, Olivier; Hodges, John R.; Halliday, Glenda M.; Topp, Simon D.; Smith, Bradley N.; Shaw, Christopher E.; McCann, Emily; Fifita, Jennifer A.; Williams, Kelly L.; Atkin, Julie D.; Blair, Ian P.; Kwok, John B. In: *Brain : a journal of neurology*, Vol. 143, No. 3, 01.03.2020, p. 783-799.
- **Emerging evidence highlighting the importance of redox dysregulation in the pathogenesis of amyotrophic lateral sclerosis (ALS).**
Jagaraj, Cyril Jones; Parakh, Sonam; Atkin, Julie D. In: *Frontiers in Cellular Neuroscience*, Vol. 14, 581950, 18.02.2021, p. 1-29.
- **Evidence for a growing involvement of glia in amyotrophic lateral sclerosis.**
Radford, Rowan A. W.; Vidal Itriago, Andres; Scherer, Natalie M.; Lee, Albert; Graeber, Manuel B.; Chung, Roger S.; Morsch, Marco. *Spectrums of amyotrophic lateral sclerosis: heterogeneity, pathogenesis and therapeutic directions*. ed. / Christopher A. Shaw; Jessica R. Morrice. Hoboken, NJ : John Wiley & Sons, 2021. p. 123-142.
- **Evidence for polygenic and oligogenic basis of Australian sporadic amyotrophic lateral sclerosis.**
McCann, Emily P.; Henden, Lyndal; Fifita, Jennifer A.; Zhang, Katharine Y.; Grima, Natalie; Bauer, Denis C.; Fat, Sandrine Chan Moi; Twine, Natalie A.; Pamphlett, Roger; Kiernan, Matthew C.; Rowe, Dominic B.; Williams, Kelly L.; Blair, Ian P. In: *Journal of Medical Genetics*, Vol. 58, No. 2, 01.02.2021, p. 87-95.
- **Genetic analysis of GLT8D1 and ARPP21 in Australian familial and sporadic amyotrophic lateral sclerosis.**
Chan Moi Fat, Sandrine; McCann, Emily P.; Williams, Kelly L.; Henden, Lyndal; Twine, Natalie A.; Bauer, Denis C.; Pamphlett, Roger; Kiernan, Matthew C.; Rowe, Dominic B.; Nicholson, Garth A.; Fifita, Jennifer A.; Blair, Ian P. In: *Neurobiology of Aging*, 16.01.2021.
- **Genetic analysis of tryptophan metabolism genes in sporadic amyotrophic lateral sclerosis.**
Fifita, Jennifer A.; Chan Moi Fat, Sandrine; McCann, Emily P.; Williams, Kelly L.; Twine, Natalie A.; Bauer, Denis C.; Rowe, Dominic B.; Pamphlett, Roger; Kiernan, Matthew C.; Tan, Vanessa X.; Blair, Ian P.; Guillemin, Gilles J. In: *Frontiers in Immunology*, Vol. 12, 701550, 14.06.2021, p. 1-8.
- **Genetic and immunopathological analysis of CHCHD10 in Australian amyotrophic lateral sclerosis and frontotemporal dementia and transgenic TDP-43 mice.**
McCann, Emily P.; Fifita, Jennifer A.; Grima, Natalie; Galper, Jasmin; Mehta, Prachi; Freckleton, Sarah E.; Zhang, Katharine Y.; Henden, Lyndal; Hogan, Alison L.; Chan Moi Fat, Sandrine; Wu, Sharlynn S. L.; Jagaraj, Cyril J.; Berning, Britt A.; Williams, Kelly Louise; Twine, Natalie A.; Bauer, Denis; Piguat, Olivier; Hodges, John; Kwok, John B. J.; Halliday, Glenda M.; Kiernan, Matthew C.; Atkin, Julie; Rowe, Dominic B.; Nicholson, Garth A.; Walker, Adam K.; Blair, Ian P.; Yang, Shu. In: *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 91, No. 2, 01.02.2020, p. 162-171.
- **Genetic counseling and testing practices for late-onset neurodegenerative disease : a systematic review.**
Crook, Ashley; Jacobs, Chris; Newton-John, Toby; O'Shea, Rosie; McEwen, Alison. In: *Journal of Neurology*, 01.03.2021.
- **Genome-wide meta-analysis finds the ACSL5-ZDHHC6 locus is associated with ALS and links weight loss to the disease genetics.**
Iacoangeli, Alfredo; Lin, Tian; Al Khleifat, Ahmad; Jones, Ashley R.; Opie-Martin, Sarah; Coleman, Jonathan R. I.; Shatunov, Aleksey; Sproviero, William; Williams, Kelly L.; Garton, Fleur; Restuadi, Restuadi; Henders, Anjali K.; Mather, Karen A.; Needham, Merilee; Mathers, Susan; Nicholson, Garth A.; Rowe, Dominic B.; Henderson, Robert; McCombe, Pamela A.; Pamphlett, Roger; Blair, Ian P.; Schultz, David; Sachdev, Perminder S.; Newhouse, Stephen J.; Proitsi, Petroula; Fogh, Isabella; Ngo, Shyuan T.; Dobson, Richard J. B.; Wray, Naomi R.; Steyn, Frederik J.; Al-Chalabi, Ammar. In: *Cell Reports*, Vol. 33, No. 4, 108323, 27.10.2020, p. 1-9.
- **Identity by descent analysis identifies founder events and links SOD1 familial and sporadic ALS cases.**
Henden, Lyndal; Twine, Natalie A.; Szul, Piotr; McCann, Emily P.; Nicholson, Garth A.; Rowe, Dominic B.; Kiernan, Matthew C.; Bauer, Denis C.; Blair, Ian P.; Williams, Kelly L. In: *npj Genomic Medicine*, Vol. 5, No. 1, 32, 07.08.2020, p. 1-8.
- **Impaired NHEJ repair in amyotrophic lateral sclerosis is associated with TDP-43 mutations.**
Konopka, Anna; Whelan, Donna R.; Jamal, Md Shafi; Perri, Emma; Shahheydari, Hani; Toth, Reka P.; Parakh, Sonam; Robinson, Tina; Cheong, Alison; Mehta, Prachi; Vidal, Marta; Ragagnin, Audrey M. G.; Khizhnyak, Ivan; Jagaraj, Cyril J.; Galper, Jasmin; Grima, Natalie; Deva, Anand; Shadfar, Sina; Nicholson, Garth A.; Yang, Shu; Cutts, Suzanne M.; Horejsi, Zuzana; Bell, Toby D. M.; Walker, Adam K.; Blair, Ian P.; Atkin, Julie D. In: *Molecular Neurodegeneration*, Vol. 15, No. 1, 51, 09.09.2020, p. 1-28.
- **In vivo validation of bimolecular fluorescence complementation (BiFC) to investigate aggregate formation in amyotrophic lateral sclerosis (ALS).**
Don, Emily K.; Maschirow, Alina; Radford, Rowan A. W.; Scherer, Natalie M.; Vidal-Itriago, Andrés; Hogan, Alison; Maurel, Cindy; Formella, Isabel; Stoddart, Jack J.; Hall, Thomas E.; Lee, Albert; Shi, Bingyang; Cole, Nicholas J.; Laird, Angela S.; Badrock, Andrew P.; Chung, Roger S.; Morsch, Marco. In: *Molecular Neurobiology*, 07.01.2021.
- **Is exposure to BMAA a risk factor for neurodegenerative diseases? A response to a critical review of the BMAA hypothesis.**
Dunlop, R. A.; Banack, S. A.; Bishop, S. L.; Metcalf, J. S.; Murch, S. J.; Davis, D. A.; Stommel, E. W.; Karlsson, O.; Brittebo, E. B.; Chatziefthimiou, A. D.; Tan, V. X.; Guillemin, G. J.; Cox, P. A.; Chatziefthimiou, D. C.; Bradley, W. G. In: *Neurotoxicity Research*, Vol. 39, No. 1, 02.2021, p. 81-106.
- **Protein disulphide isomerase (PDI) is protective against amyotrophic lateral sclerosis (ALS)-related mutant Fused in Sarcoma (FUS) in in vitro models.**
S. Parakh, E. Perri, M. Vidal, J. Sultana, S. Shadfar, P. Mehta, A. Konopka, C. Thomas, D. Spencer, J. Atkin. In: *Scientific Reports In Press*.
- **SFPQ intron retention, reduced expression and aggregate formation are pathological features of amyotrophic lateral sclerosis.**
Hogan AL, Grima N, Fifita JA, McCann EP, Heng B, Fat SCM, Wu S, Maharjan R, Cain AK, Henden L, Rayner S, Tarr I, Zhang KY, Zhao Q, Zhang ZH, Wright A, Lee A, Morsch M, Yang S, Williams KL, Blair IP. 2021. In: *Neuropathology and Applied Neurobiology*. <https://doi.org/10.1111/nan.12749>
- **The mitochondrial-associated ER membrane (MAM) compartment and its dysregulation in amyotrophic lateral sclerosis (ALS).**
Parakh, Sonam; Atkin, Julie D. In: *Seminars in Cell and Developmental Biology*, Vol. 112, 04.2021, p. 105-113.
- **The redox activity of protein disulfide isomerase inhibits ALS phenotypes in cellular and zebrafish models.**
Parakh, Sonam; Shadfar, Sina; Perri, Emma R.; Ragagnin, Audrey M. G.; Piattoni, Claudia V.; Fogolin, Mariela B.; Yuan, Kristy C.; Shahheydari, Hamideh; Don, Emily K.; Thomas, Collen J.; Hong, Yuning; Comini, Marcelo A.; Laird, Angela S.; Spencer, Damian M.; Atkin, Julie D. In: *iScience*, Vol. 23, No. 5, 101097, 22.05.2020, p. 1-27.
- **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, Flora; Luca, Alana De; Hogan, Alison L.; Rayner, Stephanie L.; Davidson, Jennilee M.; Watchon, Maxinne; Stevens, Claire H.; Muñoz, Sonia Sanz; Ooi, Lezanne; Yerbury, Justin J.; Don, Emily K.; Fifita, Jennifer A.; Villalva, Maria D.; Suddull, Hannah; Chapman, Tyler R.; Hedl, Thomas J.; Walker, Adam K.; Yang, Shu; Morsch, Marco; Shi, Bingyang; Blair, Ian P.; Laird, Angela S.; Chung, Roger S.; Lee, Albert. In: *Frontiers in Molecular Neuroscience*, Vol. 14, 627740, 27.04.2021, p. 1-18.

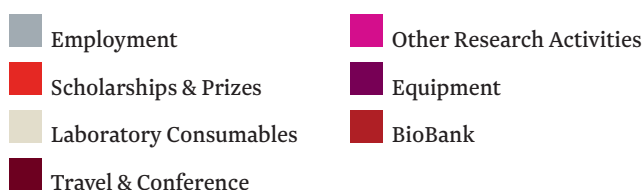
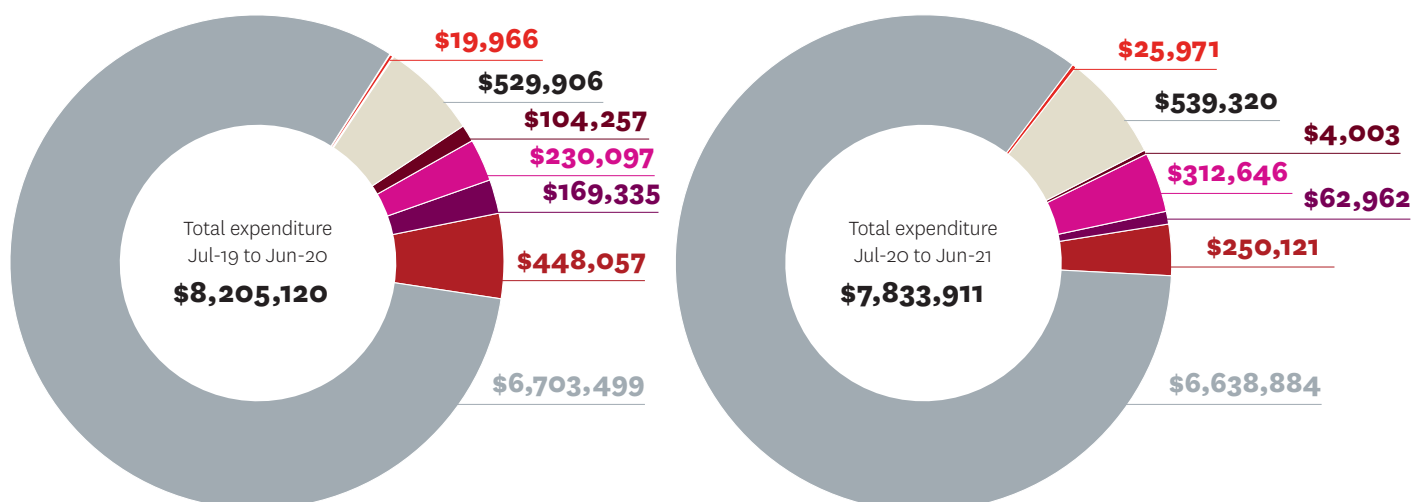
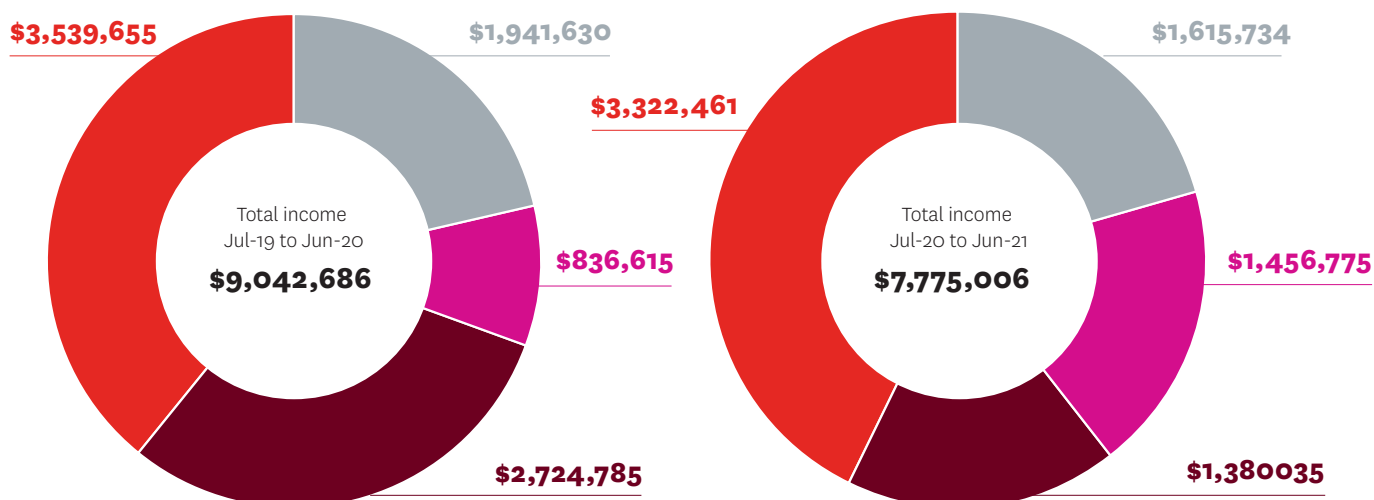
Governance structure

Centre leadership



Financial highlights

Summaries of the income and expenditure, in 2019-20 and 2020-21, for the Centre for MND Research 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 2020/2021

Our researchers at the Centre for MND Research 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	Co-Investigators	Project Title	Amount Funded	Years Funding
Fight MND	FightMND IMPACT Grant	Julie Atkin	Blair, Ian (Chief Investigator), Rowe, Dominic (CI), Lim, Edwin (CI)	Disease susceptibility, precision medicine and ALS	\$249,742.00	2
National Health and Medical Research Council	NHMRC - Investigator Grants	Ian Blair		Determining the molecular basis of amyotrophic lateral sclerosis	\$1,350,000.00	4
National Health and Medical Research Council	NHMRC - Investigator Grants	Gilles Guillemain		The kynurenine pathway in neuroinflammatory disease: translation to prognostics and therapeutics	\$1,500,000.00	4
MND Research Institute of Australia Inc	MNDRA Motor Neurone Disease Research Grants	Kelly Williams	Henden, Lyndal (CI), Blair, Ian (CI)	Comprehensive transcriptome analysis of neuroanatomical regions with variable pTDP-43 pathology in sporadic ALS patients	\$100,000.00	1
MND Research Institute of Australia Inc	MNDRA Motor Neurone Disease Research Grants	Julie Atkin	Woodruff, Trent M. (CI), Karl, Tim (CI), Craik, David (CI), Guillemain, Gilles (CI), Laird, Angela (CI)	Modulating Actin Dynamics in MND as a Novel Therapeutic Approach	\$99,324.00	1
MND Research Institute of Australia Inc	MNDRA Motor Neurone Disease Research Grants	Albert Lee		Clearance of TDP-43 by PROteolysis Targeting Chimera (PROTAC) dual targeting to treat amyotrophic lateral sclerosis (ALS)	\$100,000.00	1
National Health and Medical Research Council	NHMRC - Ideas Grants	Dominic Rowe	Goldys, E., Bush, A. I., Hutchinson, M. R. & Crouch, P. J.	The colour of amyotrophic lateral sclerosis: hyperspectral imaging cytometry of peripheral monocytes towards diagnostics and treatment monitoring	\$120,000.00	2
Blade Therapeutics Pty Ltd	Blade Therapeutics Pty Ltd	Angela Laird		Test a novel calpain inhibitor compound on zebrafish	\$85,000.00	1
MND Research Institute of Australia Inc	MNDRA Motor Neurone Disease Research Grants	Marco Morsch		The unexplored posttranslational modification (SUMOylation) of TDP43 affects aggregate formation and localisation	\$128,382.67 (\$100,000.00 + \$28,382.67)	1
Fight MND	FightMND IMPACT Grant	Roger Chung	Chung, Roger (Primary CI), Lisowski, Leszek (CI), Shi, Bingyang (CI)	Development of a dose-escalatable AAV delivery system for ALS gene therapies	\$250,000.00	2
National Health and Medical Research Council	NHMRC - Investigator Grants	Bingyang Shi		Novel nanotechnology strategies for drug delivery to the brain and preclinical evaluation of therapies	\$950,000.00	4
Fight MND	FightMND Drug Development Research Grant (DDG)	Roger Chung	Lisowski, Leszek (CI), Walker, Adam Keith (CI), Rogers, Mary-Louise (CI), Lee, Albert (CI), Morsch, Marco (CI), Rayner, Stephanie (CI)	Development of a TDP43-targeting gene therapy for ALS	\$1,000,000.00	3
Macquarie University	MQ Research Fellowship (MQRF) Scheme	Stephanie Rayner		21-24 MQ Research Fellowship (M S Rayner 133063747 IntFun)	\$50,000.00	3
Australian Research Council	ARC Discovery Projects	Marco Morsch	Dr Albert Lee (CI), Dr Kelly Williams (CI)	Microglia and the inflammation spectrum - not just good or bad	\$416,000.00	2
MND Research Institute of Australia Inc	MNDRA Beryl Bayley MND Postdoctoral Fellowship	Emily McCann		Investigating the role of complex genomic variation in MND	\$300,000.00	3
Fight MND	FightMND Drug Development Research Grant (DDG)	Julie Atkin	Woodruff, Trent M. (CI), Karl, Tim (CI), Craik, David (CI), Guillemain, Gilles (CI), Laird, Angela (CI)	Modulating actin dynamics in ALS/MND as a novel therapeutic approach	\$999,664.12	3
MND Research Institute of Australia Inc	MNDRA Motor Neurone Disease Research Grants	Ian Blair	Lyndal Henden, Kelly Williams	Genome-wide detection of short tandem repeats that are expanded in ALS	\$100,000.00	2
Hillcrest Foundation	Perpetual Philanthropic Services	Dominic Rowe		The Diagnostic Colour of Motor Neurone Disease	\$65,000.00	1.5

Contacts



MACQUARIE UNIVERSITY

North Ryde NSW 2109

T: +61 2 9850 7987

mq.edu.au

ABN 90 952 801 237

OA12512
CRICOS Provider 00002J

RESEARCH CONTACT

Centre for Motor Neuron Disease
Research

Department of Biomedical Sciences
Faculty of Medicine, Health and Human
Sciences

Level 1, 75 Talavera Road
Macquarie University
North Ryde NSW 2109

T: +61 2 9850 2776

F: +61 2 9850 2701

E: christina.cassidy@mq.edu.au

mq.edu.au/research/mnd

ADVANCEMENT CONTACT

Office of Advancement
Macquarie University

Level 2, 16 University Avenue
Macquarie University NSW 2109

T: 1800 673 662

E: mqadvancement@mq.edu.au

To make a donation, visit

mq.edu.au/mnd

**We all work together
with the one goal –
to stop MND.**

**We know it can be done,
we just need your help to
make it happen.**

