

# Brain Matters

News from the Florey Institute of Neuroscience and Mental Health



## LIGHTNING STRIKES TWICE?

A NEW COMPOUND COULD DELIVER FOR PARKINSON'S DISEASE

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## Director's Report



**W**elcome to our latest issue of Brain Matters where we again showcase the positive and lasting impacts of Florey's research.

Our cover story builds on the very exciting news reported in January that a compound developed and investigated by the Florey, in collaboration with the University of Melbourne, appears in trials to have positive impacts for those living with motor neuron disease. We're now very pleased to share the news that the same compound appears to have some efficacy in improving some symptoms of Parkinson's disease. While we are very hopeful about these developments, in the best traditions of scientific inquiry we remain cautious. These results are in a small trial and there is a long road ahead before it can be used by clinicians. Regardless, we are very proud of the achievements of our researchers and look forward to reporting on their ongoing efforts.

We have another very positive result to report. Professor Graeme Jackson and his team have received \$1 million through the Australian Federal Government's Medical Research Future Fund (MRFF) Frontier's initiative to harness next generation brain imaging technology for diagnosis and treatment of epilepsy. Professor Jackson and his team will now spend the next year developing a plan to put this big idea into action, with the possibility of another \$10 - 50 million being awarded. The goals of the project are ambitious, with the Florey seeking to dramatically improve health outcomes for the 250,000 Australians living with epilepsy, and to simultaneously create high-value jobs in Australia through leading prevention, diagnosis and treatment of epilepsy.

We at the Florey believe that every Australian living with a disease or disorder of the brain deserves the very best answers we can give them. We need three important things to achieve this - great staff and students working in strong partnerships, strong commitment to scientific excellence, and strong community supporters. I'm very pleased that we have each of these in place. Thank you for being part of our team.

**Professor Steven Petrou PhD FAHMS**  
Director, Florey Institute of Neuroscience and Mental Health

# Shawna Farquharson heads international imaging society



Shawna Farquharson, Chief radiographer at the Florey and President, SMRT.

**T**he Florey's Chief Research Radiographer based at the Austin campus in Heidelberg has been appointed President of the International Society for MRI Radiographers and Technologists.

Announced at the society's recent international meeting in Canada, Shawna Farquharson plans to continue empowering MR radiographers and technologists to actively bridge the gap between scientific advances and clinical translation with the ultimate aim to improve patient care.

"I feel extremely honored and humbled to have been elected President of the most important and influential organization for MRI Radiographers and Technologists around the globe. I see it as an opportunity to both give back to all those that have supported and mentored me throughout my career, and to pay it forward to those who will become the future leaders of our profession," said Shawna.

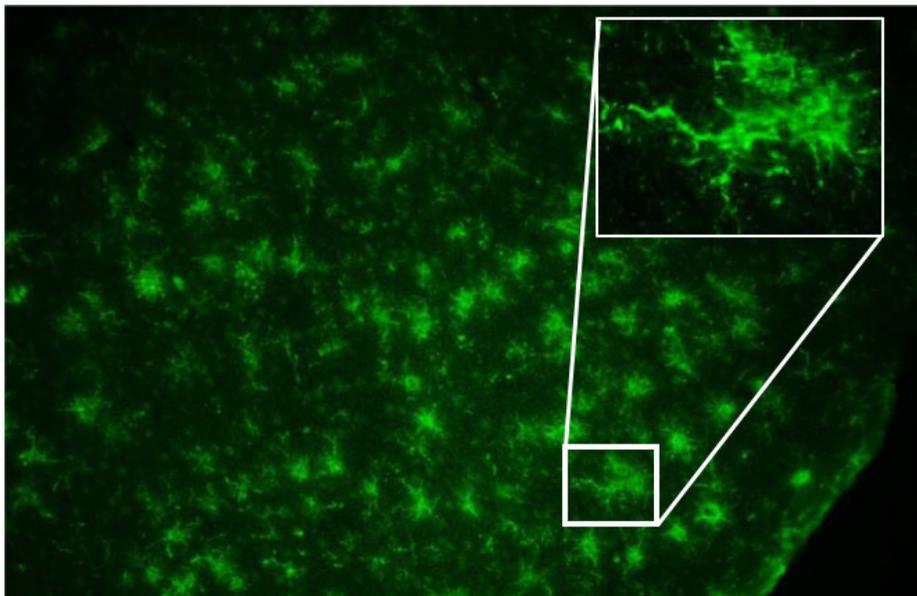
"Improving patient care is ultimately the reason why so many MRI Radiographers and Technologists around the world are so passionate

**“ I feel extremely honored and humbled to have been elected President of the most important and influential organization for MRI Radiographers and Technologists around the globe. ”**

about our profession. This is why we are so personally invested and committed to our ongoing professional education."

In her role at the Florey, Shawna is responsible for advanced brain imaging on a wide range of research projects, including study of healthy brains and a variety of clinical conditions including sleep apnea, stroke and mental health.

# Enlisting the brain's immune cells to fight multiple sclerosis



Treating microglia to reduce their activation levels could result in better outcomes for stroke recovery.

**S**pecialist cleaning cells in the brain play a key role in neurodegenerative diseases, and they may also hold the secret to new treatments for diseases like multiple sclerosis.

Professor Trevor Kilpatrick and his colleagues think the brain's immune cells, called microglia, could be the key to creating a revolutionary treatment for multiple sclerosis.

Trevor, clinical director at the Florey and a neurologist at the Royal Melbourne Hospital, has been studying a molecule produced by microglia called MERTK.

This molecule latches on to dead cells and debris in the brain and triggers microglial cells to clean them up, much like a street sweeper clears away debris following a storm.

This clean-up is a necessary first step to let the body's own repair mechanisms get to work.

"Even though the microglia don't directly coordinate the repair—other cells regrow the electrically insulating myelin sheaths on nerve cells that are destroyed in multiple sclerosis — the repair won't work properly unless the debris has been cleaned up," Trevor says.

Trevor's studies have shown that MERTK function may be corrupted in a significant proportion of people with multiple sclerosis. Injecting molecules that stimulate MERTK seems like a possible treatment, but the molecules are too large to cross the brain's protective barrier. This so-called blood-brain barrier normally functions to keep large molecules away from privileged brain tissue.

"Microglia seem to be involved in most of the degenerative diseases, but it's only recently we've been able to study them."

Instead, Trevor's team are hoping to create MERTK-producing microglia and inject them into patients. The theory is that the injected cells will migrate to the brain and help the body fight off multiple sclerosis.

At present the research is studying the effects of microglial transplants in animals, but the next step will need human cells. This is where Professor Colin Pouton from Monash University comes in.

"Colin's group are studying lab-grown microglia, produced from human stem cells. They are detailing exactly how well they take up and dispose of cellular debris. Once we're confident that the



**Microglia seem to be involved in most of the degenerative diseases, but it's only recently we've been able to study them.**



cells are behaving the way we think they will, we can try to establish a proof of principle for tests in humans."

And it's not only in multiple sclerosis where microglia are important – they may play a significant role in other neurodegenerative diseases such as Alzheimer's and Parkinson's, and brain injuries like stroke.

Dr Carli Roulston, head of the Florey's pre-clinical stroke research laboratory, is working out how microglia respond to brain injury after stroke, where these inflammatory cells serve an important role to clear away damaged brain tissue, whilst trying to preserve surviving tissue.

The microglia response however is not always a positive. 'Over-activation' of these cells can lead to the release of damaging chemicals that contribute to injury expansion.

"This inflammation hinders subsequent brain remodelling required for functional recovery after stroke. If we can coax microglia to retain their protective role in the brain, whilst supporting removal of debris, we could create an environment in the brain that was supportive to recovery after stroke," says Carli. 

# Lightning strikes twice? A new drug shows promise



(L-R): Prof Kevin Barnham, A/Prof Peter Crouch and Prof Ashley Bush hard at work with CuATSM.

**A** new drug delays the progress of both motor neurone disease (MND) and Parkinson's disease and also improves cognitive and clinical symptoms for patients according to recently announced phase I trial results. The news comes after 15 years of hard labour by a collaborative team committed to finding a cure.

Developed by scientists from the Florey Institute, the University of Melbourne's School of Chemistry and the Bio21 Molecular Science and Biotechnology Institute, the compound has dramatically improved clinical symptoms of motor neurone and Parkinson's diseases in a trial, as well as improved cognitive symptoms in people with a diagnosis of MND.

While the number of participants in each trial was small and the studies have completed just the first hurdle, the new drug is offering a glimpse of hope for two neurodegenerative diseases that devastate those affected, their families and friends.

MND, is a progressive and fatal disease. Its key hallmark is the death of the brain cells that control muscle movements, either in the motor parts of the brain or the spinal cord. This results in muscle weakness and eventually paralysis. People are commonly diagnosed in their 40s and 50s. There are no treatments or disease-modifying therapies currently available.

Meanwhile Parkinson's disease is most widely known for its progressive motor



**Like detectives, we don't really believe in coincidences.**





impairments; patients develop rigidity and difficulty initiating movements. Although treatments exist, they can become less effective over time, and do not address the underlying cellular damage in the brain.

Two separate trials, involving a total of 51 volunteers, have now shown that a therapeutic amount of the copper compound known as CuATSM had an impact in improving lung function and cognitive ability in MND and improving motor symptoms in Parkinson's, compared to predicted rates based on observations on people who didn't have access to the drug.

The people with MND who received the CuATSM compound also showed a much slower overall disease progression as measured by an international scoring method.

The MND clinical trial was led by Professor Dominic Rowe at Macquarie University, and Associate Professor Susan Mathers at Calvary Health Care Bethlehem, while the Parkinson's disease trial was performed by Professor Andrew Evans at the Royal Melbourne Hospital.

Both trials were sponsored by Collaborative Medicinal Development LLC, with support from Neale Daniher's charity, FightMND.

Professor Ashley Bush, director of the Melbourne Dementia Research Centre at the Florey and University of Melbourne, said, "Although the MND and Parkinson's trials were both phase 1, meaning we can't make any claims about treatment efficacy, the fact we see patient improvements at the equivalent doses where we saw independently validated improvements in various mouse models of both diseases gives us confidence that we are on the right path."

Associate Professor Kevin Barnham of the Florey, Associate Professor Anthony White at the Queensland Institute of Medical Research, Professor Paul Donnelly and Associate Professor Peter Crouch from the University of Melbourne, developed and tested CuATSM over a 15-year period.

Professor Barnham, head of the Florey's Neurotherapeutics laboratory, said,

"Like detectives, we don't really believe in coincidences. Taken together, the results from the two trials are very encouraging. When we began developing this compound 15 years ago we were quietly optimistic. So, while it is still too early to claim definitive success, we're doing the hard yards to discover exactly how the compound may be saving brain cells, and hope to report on this before the end of the year."

After showing its therapeutic potential for neurodegenerative diseases like MND and Parkinson's in pre-clinical models, the researchers founded a company and licensed the compound to Collaborative Medicinal Developments to take the drug into human studies.

Professor Donnelly said, "It is gratifying to see such promising results made possible by collaborative fundamental research at the interface between chemistry and biology."

The researchers plan to begin enrolment for a larger trial in late 2019 which will test CuATSM's effectiveness in MND/amyotrophic lateral sclerosis in a larger group of volunteers. 

# Sleeping our cares away

**D**r Laura Jacobson is the Florey's Head of Sleep and Cognition laboratory. She spends her waking hours considering the impact of 'sleep architecture' – how we sleep – and its links to learning and memory.

We spend a third of our lives asleep," Laura says. "It's not wasted time, it's critically important." Indeed, while we sleep our brain is busy testing connections, replaying key moments and reconfiguring itself.

While the vast majority of sleep research focuses on activating specific receptors to turn off brain cells to promote sleep, Laura is involved in a different line of research which concentrates on the orexin system in neurons that control our awake-sleep activity. Drugs known as dual orexin receptor antagonists (DORAs) target receptors that are activated by orexin when we're awake.

Laura is particularly interested in how sleep and dreaming act as mechanisms that allow our brains to dump information.

“**My opinion is that dreaming is in part a re-run of aspects of the day's memory and it's testing out the wiring.**”

Laura's research is helping us understand the way we process emotional memories and may even help us diagnose Alzheimer's disease. Although she can't perform dream analysis on animals, she can observe the associated types of neural patterns.

For example, recent research on 'place cells' shows that when an animal runs in a maze, they make a mental map of the maze as they navigate, with different cells in the brain's memory region firing depending on where they are in the maze. "We can actually see that process re-running in their brain during sleep" says Laura.

Scientists have shown that tangles of the tau protein in the brain are associated with advancing dementias like Alzheimer's disease and frontotemporal dementia. Tau build-up appears to run alongside elevated levels of orexin in the fluid surrounding the brain. Broken or reduced sleep and increased time awake is often a symptom of Alzheimer's, well before any memory issues become apparent, so Laura is exploring whether manipulating sleep using DORAs to block orexin activity, might help slow Alzheimer's progression.

"In our work with animal models of Alzheimer's disease, we are testing whether reducing time awake and increasing Rapid Eye Movement sleep can help to improve memory and slow the development of Alzheimer's. Achieving this would be a very welcome development for individuals affected by this devastating disorder."

## New research centre a boost for patient and family hope



Vice president of the KCNQ2 Cure Alliance, Sara James, with her daughter Jacqui who has been diagnosed with a rare genetic epilepsy.

**O**ver a decade of research at the Florey has led to a leading US-based pharmaceutical company basing its Asia-Pacific headquarters in Melbourne, creating hope for patients and a boost to Melbourne's growing biotechnology sector.

Praxis Precision Medicines, a biotech company born out of more than a decade of research at the Florey, will work towards delivering new medicines for people with epilepsy, autism and mental illness. Basing their headquarters in Melbourne and building an adjacent research and development centre will ensure the Florey's ongoing connections to its projects and clinical programs.

Dr Kiran Reddy, President and CEO of Praxis, who is one of the leading neuroscientists in the United States, and a successful biotech entrepreneur, said that access to skilled partners including the Florey was behind the company's decision to locate in Melbourne, which will create over 100 new jobs.

Speaking at the launch event, Vice President of the KCNQ2 Cure Alliance, Sara James, introduced her daughter, Jacqui, who was diagnosed with a rare genetic epilepsy shortly after birth. KCNQ2 Cure Alliance raises awareness and funds for research.

Director of the Florey, Steven Petrou, said the announcement was an example of how the research activity of one laboratory had influenced decisions of investors and biotechnology executives to engage more broadly across the science and medical communities in Victoria, and importantly create new precision medicine and treatments for people living with rare conditions.

"This announcement is the result of many people working together – researchers here at the Florey, Praxis, state and federal governments, the biomedical sector in Victoria, clinical partners and hospitals, and importantly community," said Professor Petrou.

Minister for Economic Development Mr Tim Pallas MP said, "More and more global players are choosing Victoria as their home base in Australia – and Praxis moving to Parkville will not only create jobs and build the economy, it will potentially improve the lives of millions of people."



Professor Christine Kilpatrick AO.

**T**he Florey is pleased and proud to welcome our newest Board member, Professor Christine Kilpatrick AO who joined the board in May.

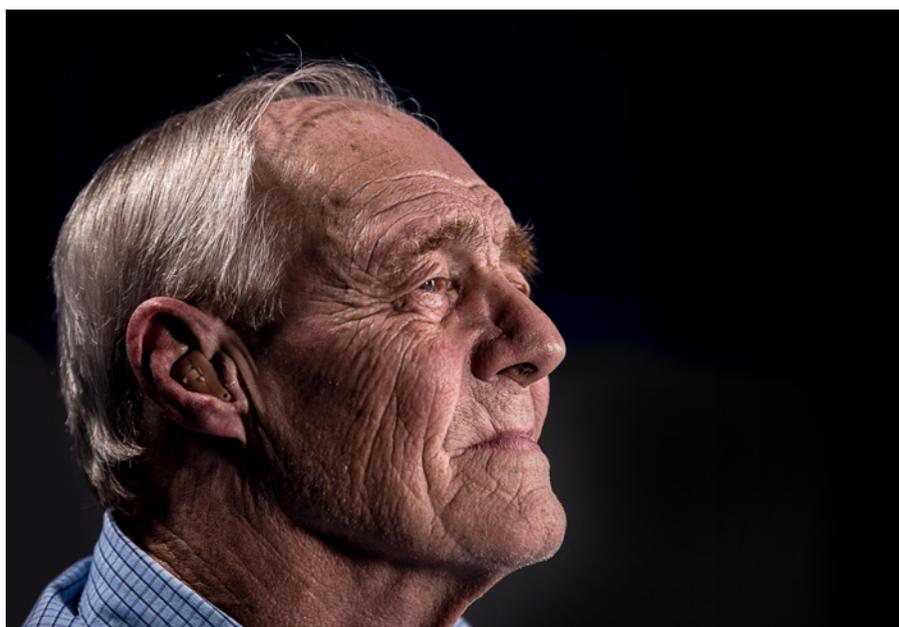
In the recent Queen's Birthday Honours list, Professor Kilpatrick was awarded an Order of Australia (AO) medal, for her "distinguished service to medicine through senior administrative roles, to the promotion of quality in health care, and to neurology".

Professor Kilpatrick has been the Chief Executive of Melbourne Health since 2017. Her previous appointments include Chief Executive, the Royal Children's Hospital from 2008 to 2017, Executive Director Medical Services, Melbourne Health and Executive Director Royal Melbourne

Hospital, Melbourne Health from 2004 to 2008.

Professor Kilpatrick is also a member of several other boards including Orygen, National Centre of Excellence in Youth Mental Health, Walter and Eliza Hall Institute (WEHI) and the Victorian Comprehensive Cancer Centre (VCCC). She was awarded a Centenary medal in 2003, in 2014 was included in the Victorian Honour Roll of Women, in 2017 was a recipient of the Inaugural Distinguished Fellow's Award, Royal Australasian College of Medical Administrators and in 2018 was inducted in the top 50 Public Sector Women.

We welcome Professor Kilpatrick AO to the Board of the Florey and look forward to benefitting from her experience and insight.



A window on the brain: New eye scan could help predict Alzheimer's risk decades before symptoms appear.

## Eyes forward for healthy brains

We have already achieved so much in the Alzheimer's space, thanks to the generous support of donors. If you're in a position to support the Florey's research, please donate to our 2019 appeal. Your generous support is still needed to continue advancing our understanding of the disease and ultimately find a cure.

**A** revolutionary new diagnostic eye test will be offered to volunteers in the Healthy Brain Project, an Australia-wide study of healthy middle-aged adults with a family history of Alzheimer's disease that aims to identify risk factors for the disease.

The research brings together Healthy Brain project investigators, neuropsychologist Dr Yen Ying Lim, of the Florey Institute of Neuroscience and Mental Health, and neurologist Dr Nawaf Yassi at the Florey and Royal Melbourne Hospital together with leading eye researchers from the Centre for Eye Research Australia (CERA).

Dr Lim said, "We are looking forward to giving our volunteers the opportunity

to trial this exciting new technology from CERA. The data we obtain will give us greater insights into the previously invisible processes happening in the brains of people at risk of developing Alzheimer's disease."

Associate Professor Peter van Wijngaarden and Dr Xavier Hadoux from CERA and the University of Melbourne developed the imaging technology. The test uses specialised colour imaging of the eye to detect amyloid build-up, a key component of the Alzheimer's disease process.

The technology is similar to that used in NASA satellites and will accelerate research efforts to delay, prevent, or even cure, the disease. Increasingly, scientists are taking a more targeted and less invasive approach to testing new drugs and treatments for those most at risk of Alzheimer's disease. Identifying at-risk people as early as possible is key to this aim.

The research team paid credit to a group of generous Australian philanthropists, including Baillieu Myer, Samantha Baillieu and Jeanne Pratt for supporting the research in its early stages. These donors had the vision to back the initial idea in its proof of concept phase.

The Alzheimer's Drug Discovery Foundation has awarded funding for the all-important research as part of its Diagnostics Accelerator program. However, the research cannot happen without your support; through your donations we can ensure this innovative project continues to deliver invaluable insights into how the debilitating disease works so that together we can find a cure. [👉](#)

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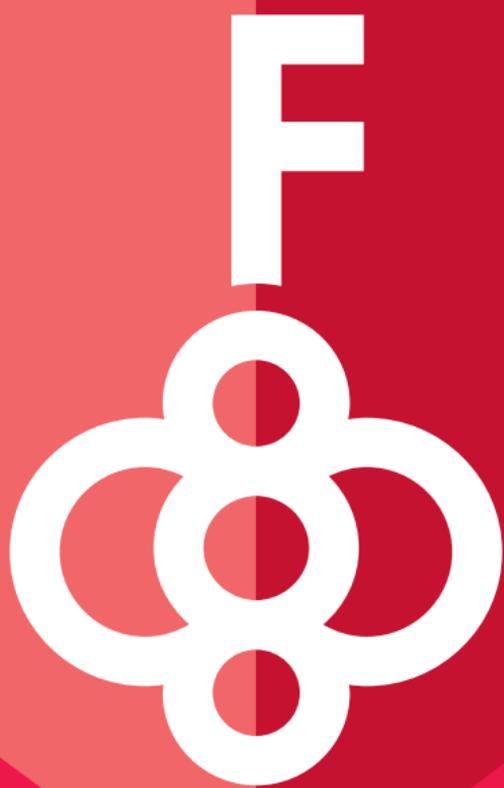
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Other ways to donate:

- Call our free call credit card donation line on 1800 063 693
- Fax your donation to us on (03) 9035 3107
- Online at [www.florey.edu.au](http://www.florey.edu.au)
- Send your donation to The Florey Institute of Neuroscience & Mental Health, Reply Paid 83037, 30 Royal Parade, Parkville, VIC 3052

Thank you for your valuable support. All donations over \$2 are tax deductible.

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# News & Events

## Join us for the Florey's free 2019 lecture series

**Please come along to the Florey's latest selection of exciting lecture topics for 2019, featuring some of our incredibly talented scientists and guest presenters. For those unable to attend on the day, please feel free to visit our website and watch the recordings from home. We look forward to welcoming you to the Florey soon.**

### Wednesday July 17 at 6pm Mental health

Hear about the latest in research on adolescent mental health, particularly in depression and schizophrenia, from Professor Chris Pantelis, director of the Melbourne Neuropsychiatry Centre.

### Tuesday August 6 at 11am The puzzle master delves into his own brain

Hear ABC Radio's David Astle discuss his Florey MRI scan during which he attempted to answer some tricky questions. Also, Dr Chris Tailby will tell us how we can locate fear, appetite and memory using MRI.

### Missing a public lecture?

Did you miss our recent lectures on Precision medicine for genetic diseases with Prof Steven Petrou, the inside story on motor neurone disease with Profs Kevin Barnham and Peter Crouch, the link between your brain and your gut with Dr Martin Stebbing or how to maintain and strengthen your cognitive abilities with Assoc Prof Amy Brodtmann?

 **Keep up to date with all our upcoming and recent lectures online:**  
[florey.edu.au/events](http://florey.edu.au/events)

## Thank You

The Florey thanks our recent donors who kindly donated \$250 or more between 6 March 2019 and 6 June 2019

Philippa Allan | RG & Lauris Allen | Rita Andre | Marilyn Armstrong | Australian NPC Disease Foundation | Kevin & Pam Barham | Lorraine & John Bates | Carmel Behan | Bendigo Stadium | Berwick Opportunity Shop Incorporated | Michael Boyt | Edward & Hazel Brentnall | Margaret Bullen | Carter Family Foundation | Keith Cattach | Faye Clarke | Anthony & Geraldine Conabere | Charlotte Cornish & Huw Apted | Geoffrey Cottrell | John Coughlan | Ernest Dawes OAM OBE | Eri Deighton | Dina & Ron Goldschlager Family Charitable Foundation | J & Dianne Dixon | Rose Downer | Kevin Doyle | Di Everingham | Rita Ferguson | Tjut Freestone | Valmae Freilich | Gemma Furtado | Tom & Jennifer Garlick | Shirley Gionfriddo | Lesley Griffin | Hay Patches and Quilters | Annette Hayes | Daryl & Roslyn Hill | Rosanna Hoad | I Y Hoolihan | Inner Wheel Club of Bairnsdale | John Izon | J & J Grants (Australian Philanthropic Services Foundation) | David Kaufmann | Peter Kelly | Pamela Killer | John Leaver | Peter Lemon | Norma Lithgow | Brian Little | Christine MacGill | June Marks | Brian Marshall | Massey Foundation | Diana Matthews | Peter McArdle | Bruce McKenzie | John Michaux | Robert Moffitt | Bruce & Judy Munro | James Munro | Pamela Newton | Helen Ng | Hon Peter Nixon AO | June Nixon-Smith | Doris Enid O'Brien | Sue O'Neill | Judith Paphazy | John Paphazy | Frances J Parris | Patricia Peck | Ron Pitcher AM | Eda Ritchie AM | John & Margot Rogers | David Shaw | Robert & Elisabeth Sinclair | Edward Stabb | Jacqueline Stephens | Richard Stradwick | Takako Subocz | Dorothy Tagg | Gregory & Wendy Taggart | Wendy Taylor | The Dowd Foundation | The Marchis Family Charitable Gift | The Valda Klaric Foundation | The Yulgilbar Foundation | Debbie & Peter Thomas | Chris Togias | Tom & Ruth O'Dea Foundation (Lord Mayor's Charitable Foundation) | Elizabeth Trevena | Kay Tudor | John Vroland | Richard & Juneth Wall | Trevor & Crystal White | Kaaren Whyte | Gart Willey | Stuart Wilson | Sineke Winter

### Donations in memory of

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Nicole Armanasco (Watling)	Robert Mau
Mark Everingham	Laurence Scott
Matthew Flahavin	Margaret Shilton
Alice Foster	George Maurice Smith
Dr Malcolm Harrop OAM	Sue Wiltshire

### Donation in celebration of birthday

Richard Murphy (70<sup>th</sup>)

### Donation in celebration of wedding

Charlotte Cornish and Huw Apted

For more information contact  
[communications@florey.edu.au](mailto:communications@florey.edu.au) or 03 9035 3000.

Find us on Facebook and Twitter at our website: [florey.edu.au](http://florey.edu.au)

The Florey Institute of Neuroscience and Mental Health conducts its research on the lands of the Wurundjeri people of the Kulin Nation.

We pay our respects to the traditional owners of this country, their ancestors, their children and the lore of the creator spirit Bunjil.

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