BIOMARKER DISCOVERY BRINGS HOPE FOR SERIOUS EPILEPSY CONDITION
Welcome to this issue of Brain Matters where we again share some of the Florey’s news from the forefront of brain science.

As we continue to be impacted by COVID-19 across the globe, I’ve been contemplating how this pandemic has in some ways brought many of the ‘behind the scenes’ scientific processes into the public spotlight. News reports tell us in excited tones of the latest developments, the occasional setbacks and time and again previously unknown heroes of the community, medicine and science come to the front to tell us of something newly discovered and renew our hope that this terrible crisis will soon be over.

At the time of writing this column, we unfortunately were unable to hold face to face events for the public. I know meeting with community members is a real source of motivation and inspiration for our scientists, so this month as I’ve been checking in with staff and students across the institute I’ve been asking what they want people living with the conditions we study to know.

Across all of the Florey’s research themes, there has been a remarkable consistency to the response – “let people know we’re still working for them”.

For those living with a diagnosis of a brain condition, or if you have a loved one who is impacted, I hope you find this very heartfelt and direct message a source of hope. The Florey has research projects on more than twenty brain conditions as diverse as Alzheimer’s disease, depression, stroke, motor neurone disease and more. This issue of Brain Matters covers just a few of the stories of people at the Institute in their relentless and dedicated pursuit of life-changing treatments for diseases of the brain and mind.

As passionate as our scientists are, we could not make the discoveries that drive impact without you. Thank you for your continued support of the Florey and shared belief that a future free of neurological conditions is possible.

Professor Steven Petrou PhD FAHMS
Director, Florey Institute of Neuroscience and Mental Health
The Florey is passionate about improving lives through brain and mind research. As part of Rare Disease Day, we shone a spotlight on some of our researchers and staff who work every day towards advancing scientific knowledge, treatments and community awareness of rare diseases.

We were proud to bring the stories of these people to the Florey’s social media audience, showcasing to the community how they work with people and families who live with rare disease and what continues to inspire them in the research that they do.

Dr Ya Hui Hung, Senior Research Officer in the Oxidation Biology Unit.

“The connection between copper and the NPC1 protein is what lead me to study Niemann-Pick Disease Type C where I am investigating a gene therapy treatment. I work closely with families of children with NP-C and the Australian NPC Disease Foundation who are incredible supporters.”

Craig Thomson, Bioresources Manager.

“My son Jack lives with Angelman syndrome, a rare neurological condition. I feel a deep sense of satisfaction supporting the Florey researchers chipping away at science, and seeing the passion they bring progressing towards discoveries that will help kids like Jack in the future.”

Lauren Bleakley, PhD student in the Neurophysiology of Excitable Networks Lab.

“The inspiration for my PhD project came from a young girl, Ebony, who has a rare and severe form of epilepsy caused by a mutation in her HCN1 gene. My research aims to determine the most effective treatments, with my dream being that she, and others like her, are able to live unhindered, healthy lives.”

A/Prof Snezana Maljevic, Head of the Epilepsy Functional Genomic Laboratory.

“SCN2A is a severe form of genetic epilepsy in children. There is still much to learn about this rare disorder. We continue to work closely with SCN2A families to investigate treatment combinations in the lab and use precision medicine approaches that have shown success in other diseases.”
Florey researchers identify biomarker to predict sudden unexpected death in epilepsy

Sudden unexpected death in epilepsy (SUDEP) affects around 1 in 1,000 people living with epilepsy each year. New findings by Florey researchers involving a gene that effects cardiac dysfunction in SUDEP could lead to the development of novel biomarkers to identify those at risk.

SUDEP most frequently occurs in young adults with severe uncontrolled seizures. A clear understanding of what causes the condition remains elusive for scientists and clinicians.

The Florey’s Professor Chris Reid and Dr Ming Soh are working with clinical and research collaborators to uncover new ways to diagnose and manage SUDEP early on.

Their work builds on earlier scientific findings from collaborators of the team who identified a range of genetic changes, known as gene ‘variants’, in people who had passed away from SUDEP.

In their latest research, the team probed to understand how variants in one of these genes, KCNH2, could affect the function of heart ion channels through which electrical messages flow to regulate heart rhythm. Variants in this gene, known as loss-of-function variants, were indeed causing dysfunction in the heart they confirmed.

“We discovered that loss-of-function KCNH2 variants play a more significant role in SUDEP than previously known. Common loss-of-function variants of this gene were expressed three times higher in a cohort who had experienced SUDEP compared to an epilepsy cohort who hadn’t. This increased to 11 times higher for rarer forms of the variant which disrupt function even more drastically,” said Dr Soh.

“We suspect what could be occurring before a SUDEP event is that the interruption of the heart’s electrical activity caused by variants in KCNH2 gene, combined with the impact of a seizure, may be causing the heart to stop beating,” she explained.

“These findings contribute a new piece to the puzzle in understanding the close connection between cardiac and brain factors that underlie SUDEP. Our discovery presents loss-of-function variants of the KCNH2 gene as possible predictive biomarkers for SUDEP which could be used therapeutically to identify those at risk of the condition,” said Prof Reid.

The team is now analysing how the brain and heart function at the time that SUDEP occurs using ECG-EEG animal models which they hope can be used to develop genetic screening tools and trial treatments to reduce SUDEP risk.

“This research is an incredible beacon of hope for people with epilepsy in the fight against SUDEP. Thank you to Dr Ming Soh and Prof Chris Reid for your tireless work. It’s a monumental achievement and brings us one step closer to ending preventable deaths from epilepsy,” said Graeme Shears, CEO of the Epilepsy Foundation of Australia.

The research was made possible by philanthropic support, including from CURE Epilepsy, and funding by the Australian Government.
For the first time in 60 years, scientists have uncovered the actions of a new metal in controlling blood vessels in the body that regulate blood pressure and blood flow. The discovery, made by researchers at the Florey and their collaborators at The University of Melbourne, opens new doors for the development of zinc-based therapies to treat cardiovascular and cerebrovascular diseases, including hypertension and stroke.

Led by Associate Professor Scott Ayton and Dr Ashenafi Betrie from the Florey, the findings showcase that important scientific discoveries can often come from unexpected places.

“We were investigating the effects of zinc-based therapies on brain function in Alzheimer’s disease mouse models when we came across surprising results. We saw that the therapy was causing blood pressure to decrease,” explained A/Prof Ayton.

After working for several years with international collaborators to find an answer, the team demonstrated that zinc levels were coordinating the behaviour of muscles that surround blood vessels to make them either relax or contract.

“This challenged what was the accepted scientific understanding that calcium and potassium were the major metals controlling this action. Our findings suggested that zinc was in fact complimenting the roles of these other metals and we were able to show that an increase in cell zinc levels caused veins and arteries to relax and blood pressure to decrease,” said Dr Betrie.

“Interestingly, we also uncovered that blood vessels in the brain and the heart were more sensitive to changes in zinc than blood vessels in other areas of the body. Why this might be in an area that we hope to study further,” he added.

While some vascular diseases were known to be a side effect of zinc deficiency, the biological mechanisms underlying this relationship had remained elusive.

“Our findings offer scientists the missing link in the correlation between zinc and cardiovascular diseases and can act to explain the complex relationship between metals and blood pressure,” said A/Prof Ayton.

The discovery presents zinc as a potential target for zinc-based therapies to treat vascular diseases such as hypertension, the leading cause of cardiovascular disease and premature death worldwide. The researchers hope that zinc-based drugs could also offer alternative options to some patients for whom current calcium-based therapeutics are not adequate.

Published in the prestigious journal, Nature Communications, the team’s serendipitous discovery is anticipated to spark new lines of research and clinical investigation to better understand and appreciate the full effects of zinc and other metals in biological functions.

Read more about this discovery by visiting the Florey’s website at florey.edu.au.
The Florey hosts advanced course for budding neuroscientists

“An opportunity that all budding neuroscientists should take if given the chance!”

That is how Associate Professor Lucy Palmer describes the Australasian Course in Advanced Neuroscience (ACAN), an intensive three-week course equipping students with advanced skills in designing and implementing state-of-the-art experimental techniques in neuroscience.

Hosted this year at the Florey, the next generation of bright minds in neuroscience will be able to learn techniques including patch-clamp recording, calcium imaging, optogenetics and pharmacogenetics.

Dr Melody Li completed ACAN in 2018 and says the experience was invaluable to her research career.

“The hands-on component was a real highlight. By the end of the course, I had been given the opportunity to perform electrode recording and calcium imaging in neuronal cultures, brain slices and animal models,” says Dr Li.

“ACAN is a great opportunity to connect with neuroscientists at different career stages and gain insights from leaders in the field. I’ve since applied the knowledge I learned to my own research in genetic epilepsies.”

The 2021 course is an initiative of the Australian Neuroscience Society and has received support from the University of Melbourne. Generous support from The Finkel Foundation has also enabled the inclusion of a dedicated 2-photo imaging / electrophysiology set up to compliment an array of in vitro and in vivo recording techniques.

Devonshire with the Director

Our second ‘Devonshire with the Director’ bequestors’ morning tea on 1 June coincided with increased restrictions in Victoria, but fortunately we had again planned to hold the event off-site by Zoom. We were able to have a Devonshire morning tea delivered to our guests at their home to enjoy during the Director’s talk.

Professor Steven Petrou regaled us with exciting news about recent Florey discoveries and our guests were able to ask questions directly after the talk.

The event was engaging and friendly and it wasn’t too much of a stretch of the imagination to picture us as sitting around a table together.

To let us know of your bequest intention, or to receive our booklet about leaving a gift to the Florey in your will, please contact Nola Wilmot, Bequest Executive nola.wilmot@florey.edu.au or 03 9035 9710.

Florey supporter Irene Court shows off her morning tea set up; scones with a side of neuroscience breakthroughs.
Meet Parool Shah, our new Philanthropy Executive

How long have you been involved in fundraising?

My involvement in fundraising started in 2005 when a personal journey led me to set up my own charity, Life’s Little Treasures Foundation. Without any government funding, the only way that I was able to make the organisation sustainable was through raising funds from philanthropy. This sparked my passion for creating positive change through philanthropy which I was then able to harness in my role at Trinity College, University of Melbourne as Business Development and Relationship Manager. To have enabled life changing experiences for students at Trinity has been personally rewarding and joyful for me, and I am very excited to take this passion to the Florey and help transform lives of people with brain disorders.

How did you first learn about the Florey?

Neuroscience has been of interest to me since it saved my life from a brain tumour. Since then, my fascination in the amazing work that is being done by the world of neuroscience has led me to the Florey and the major impact that we are creating in our society by solving some of the greatest and challenging puzzles that we are facing in humanity.

What are three words to describe the Florey?

“Inspiring, innovative, transforming”.

Do you have a message for our supporters?

I would like to take this opportunity to say a big thank you for your generosity in supporting the Florey. Without you, the Florey would not be where it is today.

We are working on some very exciting scientific projects including Parkinson’s disease, Epilepsy, Autism, Stroke and Addiction that we are seeking funding for. If you would like to hear about these projects and ways in which you can support the Florey, please feel free to contact me. I am very happy to have a cuppa, have a chat on the phone, meet virtually or in person any time.

If you have another question for Parool or would like to discuss ways you can support the Florey, please contact her at parool.shah@florey.edu.au or call 03 9035 5893.

2021 Public Lecture Series

Come along to the Florey’s latest selection of exciting lecture topics for the remainder of 2021, featuring some of our incredibly talented scientists. Lectures will be held either in hybrid format (in-person at Florey Auditorium as well as via Zoom) or as Zoom only lectures. For those unable to join us on the day, please visit our website and watch the recordings from home. More details can be found by visiting florey.edu.au/events.

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<td>11am, 12 August 2021</td>
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<td>Professor Clive May and Dr Yugeesh Lankadeva</td>
<td>The deleterious effects of open-heart surgery and severe infections on the brain</td>
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<td>Dr Ya Hui Hung</td>
<td>Developing effective treatments for Niemann-Pick Disease Type C</td>
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<td>Dr Gawain McColl</td>
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The Florey thanks our recent donors who kindly donated $250 or more between 19 January and 22 June 2021:


Donations in celebration of birthday: Jane Canaway | Mai Rogers

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The Florey Institute of Neuroscience and Mental Health
The Florey Institute of Neuroscience and Mental Health

About the Florey

The Florey Institute of Neuroscience and Mental Health is the largest brain research centre in the Southern hemisphere specialising in diseases of the brain and mind. Over 4.7 million Australians each year are directly affected by the illnesses we study. We are a world leader in discovery science, imaging technologies, clinical trials, population studies, data analytics and more. Our scientists share a common goal – to improve the lives of people through our brain and mind research.

We study:

- Addiction
- Alzheimer’s disease and other dementias
- Anxiety
- Autism
- Bipolar disorder
- Cardiovascular disease
- Concussion
- COVID-19
- Depression
- Digestive diseases
- Epilepsy
- Huntington’s disease
- Motor neuron disease
- Multiple sclerosis
- Parkinson’s disease
- Schizophrenia
- Stroke
- Traumatic brain & spinal cord injury

Contact and acknowledgement The Florey Institute of Neuroscience and Mental Health acknowledges the traditional owners of this land, the people of the Wurundjeri people and the Kulin Nations. We pay our respects to their elders, past and present. Articles and photographs in this publication remain the property of the Florey and may not be reproduced without permission. For more information please contact communications@florey.edu.au