

Brain Matters

News from the Florey Institute of Neuroscience and Mental Health



X-RAYS SHINE BRIGHT LIGHTS ON WORMS

WELCOME TO BRAIN RESEARCH AT THE FLOREY

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Director's Report



The Florey continues on its upward trajectory as we attract more researchers, publish an increasing number of influential publications and secure competitive grant funding. Indeed, the institute is a power house of productivity. A wonderful time to be able to share our successes with you, our valued donors.

While you may not be able to make it to our very popular public lecture series, I would encourage you to visit the Florey YouTube channel to watch our researchers in action. You can discover how we form memories, the latest in stroke discovery, depression and diet, and the future of motor neurone disease research – among many fascinating topics.

Florey researchers are dedicated to reaching out to our supporters. We are keen to share our knowledge and to support communities facing the challenges associated with brain diseases and disorders.

I hope you enjoy reading this edition. On page 4, our team in neural plasticity, led by Professor Anthony Hannan, describes their work into fascinating new territory. His investigation into new brain pathways could lead to therapies for depression and Huntington's disease. He has shown that a nutritional supplement alleviates depressive symptoms in a mouse model by altering a brain signalling system. With mental illnesses posing such a huge burden to society, this work shows promise as another tool in an area desperately needing a wider range of medications.



I would like to share some exciting news. Professor Ingrid Scheffer AO, has been elected as a Fellow of the Royal Society of London. This is a great honour

and we congratulate one of our most respected clinicians and one who has transformed our understanding of epilepsy. She has identified many genes responsible for this often devastating condition which opens up possibilities for new therapies which are likely to improve the lives of many affected children.

With your support, scientists like Ingrid and Tony will continue to make these extraordinary discoveries. And they will happen more quickly.

Stay warm and please keep in touch,

Professor Geoffrey Donnan AO
Director, The Florey Institute of Neuroscience & Mental Health

A Parkinson's disease trial



The Parkinson's disease PKG© watch which is used around the world.

Prof Malcom Horne of the Florey Institute has recently commenced a national study looking at a 'treat to target' approach to managing Parkinson's disease using the PKG© watch.

Parkinson's Victoria, the Michael J Fox Foundation, Shake It Up and Global Kinetics are all supporting the project.

The aim is to establish whether objective measurement aids in improved clinical care and leads to improved control of Parkinson's disease and quality of life. It will compare current standard clinical practice that patients receive from their doctors, with the 'treat to target' practice of managing Parkinson's disease. This practice asks some participants to modify their current medication so that they are using their medications more effectively, and therefore managing their Parkinson's more effectively too.

A recent Florey study published in Nature Parkinson's Disease, using objective symptom measurement, shaped the patient criteria for the treat to target study.

The study is recruiting people aged between 59-75 years old, on four or more doses of levodopa medication each day and not being treated with device assisted therapies.

People with Parkinson's will participate at ten sites across Melbourne, Hobart, Shepperton, Adelaide, Brisbane and Sydney. The study will still be recruiting participants over the next month, with a momentum to conclude the first stage of this study by the end of the year.

For more information please visit www.florey.edu.au/parkinsons-movement-trial

International Clinical Trials Day

Did you know May 20th marked International Clinical Trials Day? This commemorates the day in 1747 that Dr James Lind started his study to determine the cause of scurvy – the world's first ever controlled clinical trial. By dividing 12 sailors into six separate groups and testing the effect of providing different supplements to each group, Lind was able to provide evidence of the link between eating citrus fruit and preventing scurvy.

International Clinical Trials Day is celebrated to raise awareness of the importance of clinical trials and research in healthcare, and the Florey's Neuroscience Trials Australia is proud to continue in this fine tradition.

X-rays shine bright lights on worms



Dr Erin McAllum and Dr Simon James at the Australian Synchrotron.

Amazingly, inside every cell of the brain there is an echo of the chemistry that occurred deep underwater in early oceans of primeval Earth.

Modern day "white smokers" – towers of inorganic salts deposited alongside geothermal vents in the ocean floor – are thousands of meters under the sea. They occur when superheated hydrothermal fluid mixes with near-freezing seawater. They offer us a tantalising glimpse of structures in which life may have begun.

Of course, our brain chemistry is significantly more complex than a prehistoric pimple on the ocean floor, but the chemistry that occurred in this almost alien environment is preserved within every cell of our body, indeed it is baked into our biochemistry.

Florey dementia researcher, Dr Simon James, observes the close alignment between Earth's ancient geochemistry and our brain's

biochemistry and concludes that the two must be linked.

"The theory is that pores in the hydrothermal vent chimneys provided the primordial templates for cells," says Simon, member of the Oxidation Biology team.

"The thin mineral walls of their interconnected micropores separated the internal space from the surrounding sea water, which gave rise to pH, salt and temperature gradients mirroring those seen in modern cells. This environment allowed the creation of true, single celled organisms with their own membranes."

Some of the same ancient enzymes drive our brain cell metabolism, and many of these possess activity that mirrors, at the atomic level, the structures of the iron-rich minerals that made up these ancient vents.

"In a way, before life could leave its watery inorganic cradle and evolve into the rich and varied biosphere of modern times it needed to 'chip off' some of this ancient rock."

Simon observes the close alignment between Earth's ancient geochemistry and our brain's biochemistry and concludes that the two must be linked.

Accelerating worms at lightning speed

Meanwhile, Simon is exploiting his chemical training, and access to Australia's most powerful X-ray microscope at the Australian Synchrotron, to further interrogate iron's role in the ageing process.

"By blasting the microscopic worm, *C. elegans*, with high powered X-rays, I am able to visualise how iron reacts with other biomolecules, and ideally, how the damaging effects of too much iron in the ageing brain could be kept under control."

Lewy body dementia

Simon's colleague, Dr Erin McAllum, is also logging some serious hours at the Australian Synchrotron.

Erin researches Lewy body dementia, which can be thought of as a combination of Alzheimer's and Parkinson's diseases. Patients show a similar, though more rapid, cognitive decline as with Alzheimer's, but under the microscope, the pathology looks a lot more like Parkinson's disease.

Erin is focussing on the role of copper in the Lewy bodies, the eponymous protein clumps that accumulate inside diseased brain cells.

So specialised are the techniques required to tease apart diseases at this molecular level that Erin has been awarded a Victoria fellowship to travel to the University of Bordeaux to become versed in new chemical imaging techniques.

Upon her return, Erin will be one of only a handful of Australians able to use these techniques to measure the chemical changes occurring in diseases like Lewy body dementia, leading to new therapies for this debilitating disease that will affect increasing numbers of Australians as our population ages.

For more news of Simon's and Erin's research, visit the latest Florey Annual at florey.edu.au

Preventing the brain's decline



Professor Anthony Hannan, head of the Epigenetics and Neural Plasticity laboratory.

A molecule that has proved effective in warding off Huntington's disease in mice is set to go into a clinical trial, with hopes that it will eventually delay the onset of the devastating disease in people.

Professor Anthony Hannan and his collaborators have worked on NAC (N-acetylcysteine) in recent years demonstrating its benefits in a special mouse model of the human disease. Now, Anthony will watch with enormous interest as colleagues including clinicians elsewhere in Australia translate these Florey discoveries into long-term trials of NAC as a drug.

"Huntington's is fatal and currently incurable – we desperately need new clinical trials to find an approach to prevent and treat it," he says.

The neurodegenerative disease has three main sets of symptoms which typically appear around middle age; psychiatric (including depression), cognitive (culminating in dementia) and motor disorders in which movements become uncontrollable (including involuntary, twitching movements called chorea). Children with a parent with the mutation have a 50 per cent likelihood of inheriting the condition.

Anthony and colleagues, including Drs Dean Wright and Thibault Renoir from the Florey, found in separate studies that NAC fights Huntington's on several fronts. Firstly, it acts as an anti-oxidant. Oxidation is a chemical reaction that can produce 'free radicals', which can cause damage to cells. In this case, NAC protects against the oxidative stress that damages the 'batteries' or energy sources of cells (mitochondria).

Preventive medicine has to be the key to health in the 21st Century.

“We're targeting people who know they have the gene mutation for Huntington's and will eventually get it, but who don't have symptoms yet.”

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Their study found that, in doing this, NAC was able to delay the onset of the disease.

In another mechanism, NAC appears to act on the way glutamate regulates communication within the brain. Glutamate excites brain cells, passing nerve signals from one brain cell on to the next, but too much of it can be toxic to the neurones receiving it. The researchers found that NAC countered 'excitotoxicity' in Huntington's and helped with movement disorder and depression-like symptoms associated with the disease.

Moreover, related molecules may help patients with other neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and motor neurone disease, Anthony says.

Professor Ashley Bush, Dr Scott Ayton and others at the Florey are investigating related drugs in the context of treating dementia, their work intersecting with that of Anthony and his team.

Anthony, who has been working on Huntington's disease for 20 years, says the forthcoming trial has another unique aspect; it will be conducted on people who have the gene mutation for Huntington's but who are pre-symptomatic. "We're targeting people who know they have the gene mutation for Huntington's and will eventually get it, but who don't have symptoms yet," he says.

"Because NAC is FDA-approved, has been trialled for other disorders and is considered a safe drug and can be taken for a long time, there's a capacity to give it to people who don't yet have the disease, knowing the safety is excellent.

"We can generally predict when people will start to get symptoms from previous research and will be trying with this trial to test whether we can delay the onset of symptoms."

If the ground-breaking approach is successful it could be applied to other neurodegenerative diseases, Anthony says.

"We know with our colleagues working on dementia at the Florey that a proportion of people diagnosed with mild cognitive impairment will go on to get Alzheimer's disease.

"The kind of brain imaging being done at the Florey together with genetics and other blood biomarkers for Alzheimer's that have been developed here can all predict who will be most likely to progress to full-blown dementia – that's analogous to looking at the gene mutation, and biomarkers, in people with Huntington's.

"They're looking at ultimately targeting people even before the stage of mild cognitive impairment."

Anthony says it's vital that such approaches are taken.

"Preventive medicine has to be the key to health in the 21st Century," he says. "If we don't achieve that, every health system in the world may suffer the strain of an increasing burden of disease; 'Band-aid medicine' for people who are already sick is necessary but not sufficient in the long term. It's just not a sustainable approach to optimising life-long health and ageing across our whole population in the decades ahead."

Further funding is still being sought for the NAC trials, which are now in the design phase. 📄

International push to tackle seizures



Farewell to Professor Quentin Pittman who is returning to Canada.

Visiting researcher Quentin Pittman will return to Canada this month after nearly six months – and a fruitful exchange of ideas and knowledge – at the Institute.

Quentin, Professor of Physiology and Pharmacology at the University of Calgary and the Hotchkiss Brain Institute, has been a guest of Professor Steve Petrou's Ion Channels and Human Diseases laboratory. The Florey and the Hotchkiss are partner organisations.

"My lab in Calgary is interested in the influence of inflammation on the brain," Quentin says. "One aspect of this is the interaction of inflammation with seizure activity – Steve Petrou's and Chris Reid's laboratory is world renowned in epilepsy research. I was interested in coming here and learning about their approach to studying epilepsy and looking at ways our work might complement each other for future studies," he says.

Inflammation is just one of a number of research areas for which Quentin is recognised internationally. He and his research team have also been interested recently in understanding the mechanisms underlying co-morbid behaviours during inflammatory disease.

He has published more than 300 scientific articles that have been cited nearly 15,000 times, and has been the recipient of many awards and recognitions, including Fellowship in the Royal Society of Canada and to the Canadian Academy of Health Sciences.

Quentin, who has delivered a number of lectures about his work to other groups at the Florey and has addressed the whole institute, is leaving "regretfully" at the end of June. But, "I can see this will be the start of lots of interesting collaborations," he says. 🇺🇸

Predicting the impact of a stroke

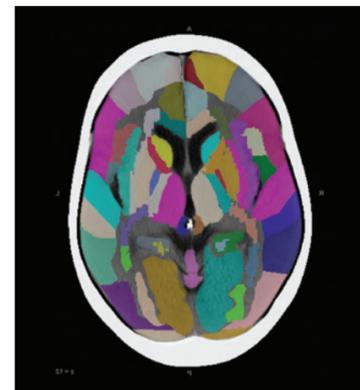
Being able to predict the outcome of stroke soon after diagnosis has always been difficult for clinicians and health carers. Damage to the brain is notoriously difficult to predict and those involved in caring for stroke patients are always very cautious in their advice.

So the development of a stroke atlas is exciting and yet another initiative of Florey researchers to influence and improve global health care.

Those involved in the long road of rehabilitation for stroke patients could particularly benefit from a guide so they can tailor treatment to individual patients and reduce the awful uncertainty that goes with the disease. Until now, having an effective and inexpensive imaging-based tool to guide health carers and researchers was a wish rather than a reality.

Dr Tina Kaffenberger and her colleagues have developed an important first step towards developing such a tool which could be used around the world.

"For any kind of predictive model, we're interested in the location of the stroke and how this relates to the final outcome for the patient. We could say, for example, 'If the stroke has spared this area of the brain, this patient will be able to walk again'," says Tina who is a member of the AVERT stroke rehabilitation group at our Heidelberg campus.



An image from the developing Stroke Atlas.

"To do this we need a standardised atlas so that we all speak the same language when we define these brain areas."

For the first time, Florey researchers have created a whole brain atlas based on an imaging template. They have collated routine CT images from the brains of hundreds of stroke patients.

This atlas allows analysis of big datasets to improve prediction tools for stroke patients. "In the longer term this could help to direct therapies in a better way and personalise them," Tina says.

"While the motor cortex is directly related to motor function for example, higher cognitive tasks such as long term memory, attention or decision-making are spread around the brain," she says. 🇺🇸



Dr Tina Kaffenberger, a member of the AVERT stroke rehab team.

A powerful alliance



“ Thanks for your support! ”

Darren Dye CEO of Pharmacy Alliance.

Some companies sponsor sport teams, others like to add their corporate name to the arts. Pharmacy Alliance CEO Darren Dye went a different path, deciding to become a corporate partner with the Florey, helping to fund our world class research in neuroscience and mental health.

It's a quiet yet vital partnership, in line with this major Australian enterprise. Darren's corporation has 580-member pharmacies and is emerging as a powerful consumer brand (as Alliance Pharmacies). He and his management team are not in the business for fame, they're in it to make a difference.

'I feel a great deal of both personal and professional pride for being able, in some small way, to support the work of these incredibly talented people at the Florey,' he told Brain Matters. 'Their work is truly inspirational and often world leading and it's amazing to play a very small part in this.'

'They (the Florey scientists) work across different parts of brain and mental health, which we find really interesting. At Alliance Pharmacies, we want to take our pharmacies into a space of being leaders around mental health, so they're a great fit for us in terms of being partners, as a corporate sponsorship.'

Darren said he was inspired by the sheer passion of the Florey professors and researchers who speak at the Foundation's Brains Trust events, of which he is a regular and enthusiastic attendee.

'I really enjoy those Brain Trusts dinners,' he said. 'The speakers are incredible. Some of those professors who speak are absolutely fabulous. In fact, a Florey stroke expert, Professor Vincent Thijs, is to speak at our company's conference later in the year. Not only is their work inspiring, and their knowledge obviously second to none, but it's their passion as well. I mean, these people are so engaged in their speaking because it's real; it's what they do every day.'

Asked which areas of Florey research most appealed to him, the Pharmacy Alliance chief exec didn't hesitate. 'I think the concussion work is really interesting, around sport,' he said. 'I think the Florey is doing some amazing work around that. I know they've got some new technology that is world leading in that space, so they're doing some really great work there.'

To learn more about the Brains Trust, contact Louise Holmes at 03 8344 0678 or email elouise.holmes@florey.edu.au 🇺🇸

Hello from our new bequest manager



Meet our newest team member, Kern Mangan-Walker.

I'm a new addition to the Florey team, joining as the Bequests, Alumni and Donor Relations Officer.

Over the last eight years I've gained a wealth of experience working with charities to improve their income streams and engage their most valued supporters, primarily through relationship fundraising, major gifts, bequests, stakeholder management and effective communications. Throughout this time I've worked for organisations as diverse as the Asylum Seeker Resource Centre, Oxfam, Anxiety New Zealand, the Australian Youth Climate Coalition and Ronald McDonald House. As a result, I am keen to help people connect with the causes they most care about, and to help them contribute to solving global issues.

My role at the Florey is to help you, our valued donors, to engage in our crucial work. Perhaps you would like to leave a gift in your will, join our alumni (for those who previously studied and worked at the institute) or to see your philanthropic visions fulfilled. I look forward to helping our supporters create a meaningful journey that deepens your engagement and knowledge. It is essential that I help donors to experience the satisfaction of creating real impact.

My experiences have allowed me to witness the life-changing power of giving and the significant impact it can have, both on the donor and the cause itself. I am excited about the opportunity to connect our supporters with the Florey's ground-breaking research and to see them deeply inspired by doing so.

To contact Kern, please email: kern.manganwalker@florey.edu.au or call 03 8344 2113. 🇺🇸

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- Online at 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 are tax deductible.

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News & Events

Public lectures

While our 2018 public lectures are booked-out, it's worth going on our Eventbrite waiting list as we often release more tickets due to cancellations. But don't worry if you can't make it! Each is recorded and can be viewed on our Florey YouTube channel or via our Facebook page under 'events'.

Lectures coming up:

What's behind the rise in autism

- What role does the environment play?

Facilitator: Dr Wah Chin Boon

Date: Tuesday, 26 June

Time: 11am

What causes Alzheimer's disease?

Two specialists in the field go toe to toe to convince you their theory will cure dementia.

Facilitators: Dr Scott Ayton and

Dr Yen Ying Lim

Date: Wednesday, 27 June

Time: 6pm

Current and emerging treatments for Parkinson's disease

From the bedside to the bench.

Facilitators: Associate Professor David Finkelstein and a nurse dedicated to Parkinson's research

Date: Wednesday, 11 July

Time: 6pm

Current and emerging treatments for drug addiction

Hear from one of Australia's leading authorities in alcohol and illicit drug dependence.

Facilitator: Professor Andrew Lawrence

Date: Tuesday, 7 August

Time: 11am

Nature, nurture and neuroplasticity

How cognitive activity, exercise and stress influence brain health and disease.

Facilitator: Professor Anthony Hannan

2 sessions due to popular demand:

Date: Tuesday, 4 September

Time: 11am

Date: Wednesday, 5 September

Time: 6pm

Are you interested in discovering more about the Florey online?

We have redesigned our website with you, our valued supporters, in mind. Find information on the research we do, read our latest news, watch one of our public lectures or donate online.

Check it out at florey.edu.au

Thank You

The Florey thanks our recent donors who kindly donated \$250 or more between 13 Feb 2018 and 04 June 2018

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For more information contact the editor,
Amanda Place: amanda.place@florey.edu.au or +61 411 204 526

Find us on Facebook and Twitter at our website: 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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