TACKLING CONCUSSION
Collingwood star Travis Cloke is helping the Florey promote brain research.
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SPIDER VENOM TO TREAT EPILEPSY
A creepy but brilliant solution.
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MOVING WITH THE POWER OF THOUGHT
A bionic implant translating brain signals into messages for artificial limbs.
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Welcome to the Florey’s latest - full of scientific highlights from the past year. While some 600 people contribute to the Florey’s brain research, it is always inspiring to stand back and marvel at the depth of knowledge and the commitment displayed by our talented scientists. We are a united and determined lot, committed to improving the human condition through neuroscience. Many of us feel a deep sense that we are in the right place at the very right time. There is no doubt that the brain is the most exciting organ to be investigating in modern medicine. Around the world, neuroscientific discovery is advancing at a cracking pace.

When we expand our focus beyond our laboratories and consider the contribution of neuroscience to the Australian population, there is much to celebrate.

As Australia develops a more sophisticated economy, it is worth noting that the sciences – physical, mathematical and biological – support more than 1 million jobs, or 10 per cent of our total employment.

The benefits are of course measurable in dollar terms but once we add the human factor, the impact is truly immeasurable. Medical research changes lives – not simply one person at a time but across entire populations. We find the causes of diseases; we discover medications to prevent or treat; we investigate the way the human mind behaves and we seek ways to modify and repair.

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The Florey has enjoyed another year of discovery and progress to help people. Our scientists have weathered the intractability of declining government funding. The National Health and Medical Research Council (NHMRC) is funding just 14 per cent of the projects it deems worthy of support. This means brilliant research programs cannot proceed. Despite this environment, we have secured several large NHMRC project and program grants that will offer a level of security to individual teams as they investigate stroke, Alzheimer’s and other diseases including motor neurone disease.

We are determined to produce exceptional science. We are always looking further afield for funding, recognising the fragile nature of government support.

The US Defense Department, through its Defense Advanced Research Projects Agency (DARPA), has been a key source of funding for brilliant projects that ‘think outside the box’ and often involve bionics. Enormous potential is realised and truly novel thinking pays off. These projects are powering ahead. The story on page 19 showcasing a start-based electrode to help paralysed people move their limbs is a case in point.

Another DARPA grant seeks to understand the role of the brain in gut disease, with the aim of inventing a bio-electronic implant to treat inflammatory bowel diseases and post-traumatic stress.

We are extraordinarily grateful to our philanthropic partners, Trusts and Foundations, and valued donors who help us take our discoveries beyond the basic to the exceptional. Without your support, we simply could not operate at an international level.

While there is great excitement and hope for the Medical Research Future Fund, it remains exactly that, a fund for the future. We hope the Federal Government continues to build the endowment, as promised, so it delivers realistic funding by 2022. If fully executed, this $20 billion fund will change the face of medical research and will propel Australian research in a dramatic way, attracting talent and securing our own as we seek healthier lives for people across the globe.

Once again, the Florey has been named as the home of Australia’s most cited neuroscientists – Professors Colin Masters and Adlrey Bush. They lead a team that includes several Florey Honorary professionals who set the pace in the field of Alzheimer’s disease and mental illness. Collaborations with colleagues in nearby hospitals and research facilities build a dynamic environment for discovery while improving patient care.

Finally, we would like to acknowledge the enormous efforts of the Florey Board during a time of consolidation and growth. Also, thank you to the Foundation Council members who have worked with our fundraising team to build our profile and to generate interest in our work. Thank you, also, to our dedicated scientists and our generous supporters.

Please enjoy reading this magazine and know you help make discoveries happen.

Breakthroughs in Brain Health Are Within Sight.

Our 20-year plan aims to:

- Diminish the scourge of dementia
- Prevent stroke and limit its impact when it does occur
- Reduce the incidence and devastation caused by mental illness
- Identify and help those genetically prone to epilepsy.
NEW TREATMENTS

BRIAN STEPHENS

These days, he focuses on ways to reveal the signalling laboratory.

Dr Jason Howitt from the Florey’s protein trafficking and development of a technique known as atomic and his contribution to modern analytical techniques is profound. His depth of experience in atomic chemistry punctuated by creative invention as he has human disease.

At the same time, the head of research at the Royal Children’s Hospital, Dr David Danks, was treating a young baby with fine, silky hair who presented with developmental and neurological defects. Dr Danks immediately identified the baby as having Merkus syndrome - a known condition with an unknown cause.

One afternoon, Dr Danks was having lunch with a mate, Dr Mort Gillespie, from the CSIRO’s wool division. Dr Gillespie described the problem he was having with the fine, silky, weak wool in copper-deficient sheep. Dr Danks raced back to the hospital and spoke to Brian who was making the first measurements of trace metals in patient samples.

Brain showed that the child’s copper levels were critically low in blood samples, but were off the charts in a gut biopsy. This suggested that Merkes disease was due to copper being unavailable for use by the body, as it was trapped in the gut lining.

Absorption spectroscopy had proved its worth in the clinic, and its future as a medical research technique was assured.

In a key and novel finding, Florey researchers have found that serum zinc is low in Alzheimer’s patients. So, are people with Alzheimer’s zinc deficient, or is zinc just difficult to measure? Brian has developed a method to quantify micro amounts of zinc and, with his colleagues, will soon compare results from stored patient samples from a number of combined studies, which together comprise one of the biggest collections in the world.

Brian says, “I still love coming in to work and being surrounded by these young, enthusiastic, and extremely bright young minds. I’m glad to contribute to our knowledge of the disease processes causing Alzheimer’s and other neurodegenerative conditions.”

The head of the metalloproteomics group, Dr Blaine Roberts, is grateful for Brian’s depth of understanding. “To have someone who was instrumental in developing one of our central technologies is an enormously valuable resource. There is nothing that Brian can’t tell you about measuring metals. If we have a problem, it’s extremely likely Brian has been there, done that. He’s also a great example that age is no barrier!”

Brian is content with his daily routine and plans to continue making his way in to the Florey, “off the charts in a gut biopsy. This suggested that Merkes disease was due to copper being unavailable for use by the body, as it was trapped in the gut lining.

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Brian is content with his daily routine and plans to continue making his way in to the Florey, enriching us with his experience, wisdom and gentle humour.
It was in almost my first week," Paul recalls. "He’s dead!’ because he was lying there with his eyes open and he wasn’t breathing. I had no idea what to do. Anyway, he woke up – which was a surprise to me - and we took him off and that started it.

I began asking some of the more experienced team doctors around the compartment: what do you do with these guys? How do you manage them? They had random ideas and points of view: put him back on, put him in the forward pocket, give him a week off..."

As a naturally curious medic, Paul found these responses unsatisfactory and so he began to read. "I reckon it took me 10 years to really start to make sense of the reading and to get to the guts of the literature and what was wrong with it. It was the starting point for me to do some proper research," he says.

Fast forward to the present day and Paul is tantalisingly close to answering why a long ago ruckman appeared to be dead – but wasn’t. When you read articles or studies about concussion, it is notable how often you read terms like ‘it is generally believed’ or ‘it is commonly thought’ but Paul and the Florey team say they could be about to end the speculation. They hope to publish the science of concussion, conclusively, in the next couple of years.

“We’ve spent a lot of time looking at (brain) imaging, which is one of the Florey’s strengths,’ he says. “Using AFL footballers predominantly, we’ve found some specific abnormalities that we think are the basis of the problem. You know, the bigger point in the brain, as it were, that turns on or off symptoms. Then we can track that with somebody who is concussed, day-by-day and week-by-week, we can track that to see when they are normally again.

“So far, it seems to be a fairly consistent finding. It’s exciting. It means we might be able to actually offer an x-ray that tells us the answer as to whether someone is ready to resume sport safely or not.

“It’s a matter of trying to put the science in place. That scientific data comes from a variety of sources. Some of it is imaging, some of it is blood testing, some of it is brain biopsies and all kinds of things. But it’s all focused on identifying the actual problem and working out how quickly can they recover. Can we put people back out there safely, if at all?

“From a scientific perspective, we’ve scanned a small number – we’re talking about 20 or 30 subjects – and we need to expand out, lock in the results and see if groups around the world can reproduce our findings, to prove that it’s not just a spurious discovery.”

The work is not just for elite footballers. “Think about the numbers,” Paul says. “In Australian football, you have roughly 700 elite athletes playing AFL, but you have 400,000 community players, and then school players after that. The bulk of people who need good safe guidelines are the community players, not the elite. We work a lot with the elite athletes because we have good access to them, and video of the injuries. There’s good baseline testing in presaison. We don’t have that luxury at a community level but it means we can test out protocols and we can see what works and doesn’t and try to translate that.”

The Florey’s work comes during a time of increasing worry for the sporting world, especially as a rising number of former professional athletes have been found to suffer from a degenerative disease of the brain identified as chronic traumatic encephalopathy (or CTE). In the United States, a class action by former players, concerned about long-term brain damage, was immediately settled by the National Football League (NFL), while the National Hockey League (NHL) is preparing to go to court to fight a class action by former ice hockey players.

Paul remains sceptical of the simplistic view that the number of concussions suffered in a sporting career results in long-term brain damage. Always coming back to the science, he and his team instead work diligently to strip away the other potential factors that cause any ageing brain to deteriorate, like genetic disposition, or lifestyle damage (drugs and alcohol, for example). concussion, and any resulting potential damage, must be scientifically revealed, instead of being ‘anecdotal’ as it is now. “In the United States, participation levels, like in the NFL’s Pop Warner junior leagues, are dropping something like five per cent per year because of the fear. Now it may turn out that it’s absolutely correct that there is something to worry about but my point is that we don’t have the data to prove it. It’s not really a scientific statement. It’s more of a belief system. We’re trying to put in place scientific structures.”

As part of this work, Paul says the Florey team has worked closely with AFL footballers, past and present, conducting highly sophisticated scanning, blood testing, genetic testing, bio marking and other testing to pinpoint the exact damage a concussion causes within a brain.

He hopes to develop a ‘Brain Passport’, so that athletes can have all their scans and concussion history in the one place, electronically stored, for their entire career from junior development squads through to retirement. He also hopes to develop robust, clear scanning and diagnoses for concussion so doctors can declare with confidence when a person has sufficiently recovered from a concussion, when they can resume sport, or when they need to retire.

Jockeys are also demanding attention from the Florey team. Falling at high speed from fast moving horses, into fences, the legs of other horses or onto hard turf pose great risks to the brain. Paul says jockeys have concussion rates 100 times higher than Australian football players, who in turn have the highest concussion rates of any professional team sports. “If you compare jockeys to NFL footballers, you are talking about a 500 times greater risk,” he says.

“Furry group is going to show long term problems, it’s going to be jockeys, and we’re working with a population of jockeys, applying the same imaging protocols (as the Florey’s AFL study). The jockeys are a refined population so we’re looking at the same things. If we can reproduce it there, and with rugby players and other populations, it will all start to make sense.”

At the Florey, a team committed to trying to understand the mysterious and high profile issue of concussion is starting to feel those flutters that accompany a major development.

The Florey's concussion research team is determined to protect the brains of senior and junior AFL players, including young kids and those in the new senior women’s league.

We know concussion is a common injury in collision sports so the safe and careful management of the condition is critical in preventing short and long-term health complications.

The institute has a memorandum of understanding with the Australian Football League (AFL), signed in 2012. It recognises the importance of the issue and the need to develop a world-leading research program to inform clinical management of its players.

When fully funded, our research will provide essential guidelines and knowledge to current athletes, retired players and, indeed, parents of children playing AFL.

Further funding is required to develop the research program – an estimated $1 million per annum over three years – if we are to influence the safety of players.

We are already actively engaged in brain injury research with other sports, as well as investigating aspects of road trauma and defence force injuries in Australia, Europe, Canada, and the USA. The Florey is an emerging key player in a world-wide, integrated program to protect brain health.
The Florey is home to an interesting mix of clinicians and medical researchers who collaborate on a daily basis. So when Dr Yen Ying Lim chatted to Dr Scott Ayton about research into dementia, a serendipitous meeting of minds occurred.

The result? A new lead to develop a diagnostic tool kit for Alzheimer’s, and a fresh approach to drug treatments for this awful disease.

Dr Yen Ying Lim is a neuropsychologist and came to the Florey with an interest in the cognitive abilities of people with dementia. Her passion is to work out what’s happening at the nexus of the genome and the mind – why do some people with dementia decline so much faster than others, when they first present with very similar symptoms and case history?

Dr Scott Ayton, on the other hand, works ‘from the ground up’. He is a molecular neuroscientist working with Professor Ashley Bush on the biochemical events underlying Alzheimer’s disease, examining the role played by biological metals like iron, copper and zinc, in the progression of the disease.

Both are members of the Australian Imaging, Biomarker and Lifestyle Flagship Study of Ageing (AIBL). Launched in 2006, it is the largest study in Australia seeking to discover which biomarkers, cognitive characteristics, and health and lifestyle factors lead to Alzheimer’s disease. More than 1100 older Australians are being observed as they age. Some will develop Alzheimer’s and others will not.

Their shared interest centres around the APOE gene, which comes in three flavours – E2, E3 and E4. Yen had access to all the AIBL participants’ APOE status, and observed that for cognitively normal individuals with a high level of amyloid beta in their brain, those carrying the E4 variation of APOE suffered declines in memory, language and cognition faster than those not carrying E4, even if they had a comparable amount of amyloid beta.

Yen says, “In fact it turns out that, aside from your age, your E4 status is the biggest risk factor for developing Alzheimer’s, dwarfing all other measures.”

Scott, on the other hand, was looking at a possible interaction between APOE and the levels of an iron-associated protein, ferritin, in the brains of patients with Alzheimer’s. Using samples from the US-based Alzheimer’s Disease Neuroimaging Initiative (ADNI), Scott showed that high ferritin levels in the cerebrospinal fluid closely correlated with brain wastage and lower cognitive ability in Alzheimer’s patients.

It predicted the progression of patients with mild cognitive problems – confusion, language difficulties and minor memory lapses – into full-blown Alzheimer’s disease. Scott also observed that people carrying the E4 variant of APOE have a 20 per cent elevation in their brain iron content. This raised the intriguing possibility that the E4 variant was driving high iron levels in the brain, which would correlate with the cognitive declines that Yen was observing in patients with Alzheimer’s.

Yen’s research had turned up another genetic curiosity. Brain Derived Neurotrophic Factor (BDNF) provides growth support to brain cells. People can have a naturally arising mutation in the BDNF gene, which means one or both copies of the gene contain a ‘Met’ mutation where a ‘Val’ should be. Yen showed that carrying this Met mutation resulted in faster cognitive decline, accelerating the failure in episodic memory associated with E4 status by up to seven years.

Intriguingly, Scott and Yen have now shown that the BDNF-Met mutation may also be linked to higher than normal iron levels in the brain.

To increase the power of their proposed study, Scott and Yen plan to combine the AIBL and ADNI samples, as well as add in a new cohort from a large Swedish study, to bring the total patient numbers to well over 1000 participants with Alzheimer’s.

“We really want to understand how these genetic cards that people get dealt influence their rate of cognitive decline if they get Alzheimer’s disease,” says Yen. Scott adds, “If we can uncover the underlying molecular pathways that are driven by these genetic changes, we can start to develop really targeted new therapies.”
The success of the Florey’s motor neuron disease (MND) research has attracted generous supporters including Shane Watson, Dr Ian Davis and former Melbourne Football Club champion, Neale Daniher. Neale, Shane and Ian are making great strides in raising public awareness - and donations - to aid our search for a cure.

Neale’s advocacy has taken public awareness about motor neuron disease to new heights – through the ‘Big Freeze at the G’ in June and a world record achievement at Etihad Stadium for the most people simultaneously taking the ‘ice bucket challenge’.

Neale says, “Every dollar raised will be used to continue the fight against ‘the beast’ by backing the work of researchers like the ones at the Florey Institute.”

It is a brutal disease. Patients initially experience weakness in their hands or feet as nerve cells begin to die. The motor neurons controlling muscles deteriorate throughout the body until the patient can no longer swallow and finally, breathe.

The Florey’s novel, international, collaborative research effort is headed by Dr Brad Turner, who leads a team of enthusiastic and dedicated research scientists, clinicians and PhD students. Recent results emerging from the lab bench are extremely encouraging.

By adding a protein, SMN, that nourishes motor neurones back into a mouse model of MND, Brad’s team has been able to prolong the lifespan of these mice by over 10 per cent. This finding is being replicated in another MND mouse model to ensure the results are robust.

Other exciting developments in the pipeline include using an immune system modulator to treat MND mice, and eventually delivering therapeutic proteins to damaged motor neurones by using genetically engineered antibodies - the body’s own chemical delivery system.

Brad’s team seeks to combine gene and neurotrophic therapies to improve motor neurone health and connections to muscle in preclinical MND models. Importantly, these therapeutic agents can be rapidly adapted to human studies, accelerating clinical development.

As well researching the molecular events that might lead to MND, the Florey is conducting a number of clinical trials in MND. This work is being performed by Neuroscience Trials Australia, the Florey’s clinical trials platform and led by Dr Tina Soulis.

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“We are currently running three separate MND trials which will recruit over 100 participants,” Tina says.

“One of the most exciting trials will aim to determine whether the antiretroviral combination therapy, used to combat HIV, might be useful in reducing the debilitating symptoms of MND and delaying disease progression, while another looks at whether altering copper levels in the cells might have a beneficial effect.”

Great strides have been made with genetic and environmental advances continually emerging. The Florey recognises and thanks those who are helping Brad’s lab in their quest for a cure.

Dr Ian Davis, Maree Edwards MP, Neale Daniher and the Premier Of Victoria, Daniel Andrews.
We’ve long believed that DNA predetermines who you are, but can your parents’ experiences be inherited along with their genes? The relatively new field of epigenetics investigates how information from the environment can affect your genes. It’s one of the fastest growing, most exciting areas of science today and the Florey is pushing at the frontier of this largely unknown field...

Epigenetics, which means “above or over” the genome, is the mechanism by which a particular gene is emphasised or not, that can lead to long-term changes in how the gene is expressed, according to Professor Anthony Hannan, who heads the Florey’s epigenetic research effort.

“It’s like an encyclopaedia in which each gene is a word, made up of letters of DNA, that can be highlighted, italicised, underlined or marked in bold by epigenetic modifications,” Anthony says.

Anthony’s Neural Plasticity laboratory focuses on understanding gene-environment interactions. His team has been investigating transgenerational epigenetics - how major environmental factors and the impact of a range of experiences on a parent may be transmitted down through the generations. For Anthony and colleagues, the question is not nature versus nurture but the bridge between them.

The researchers, including Drs Annabel Short and Terence Pang, and Katie Fennell, have focused on epigenetics work in sperm and lead to changes in the offspring embryo, a brain function and behaviour.

“We have evidence that this occurs through epigenetic information in sperm that changes the development of the offspring embryo, its brain function and behaviour.”

For Anthony, such research is a natural progression of his lab’s groundbreaking work into neural plasticity and the effects of environmental factors on the brain.

“Focusing on environmental exposures of fathers, and epigenetic effects on their offspring, is a very new area,” he says.

The team has just discovered that raising stress hormone levels in male mice – by adding the hormone to drinking water – led to changes in behaviour in offspring in ways that are linked to a predisposition to depression and anxiety disorders, and possibly other brain disorders.

“We have evidence that this occurs through epigenetic information in sperm that changes the development of the offspring embryo, its brain function and behaviour.

“It’s very early days but there is evidence that this can happen in humans.”

“These environmental exposures to chronic stress may not only increase the incidence of certain psychiatric and neurological disorders in men but it is possible they could increase the predisposition in their offspring - and that has major implications for public health.

“Chronic health problems could set up a future epidemic in the next generation. We urgently need to understand it, and how, this occurs in humans.”

Studies after particular events in history have shown that stress or trauma can affect subsequent generations in various ways. The Dutch famine in 1944 shaped the DNA of the grandchildren of adults affected by it (they were significantly underweight), and babies whose mothers were traumatised by the 9/11 disaster while pregnant were more stressed than usual in infants.

Anthony says that finding the precise mechanism that causes epigenetic changes may lead to ways of preventing it from happening in subsequent generations.

“If you know the way the negative effects of experience are being transmitted to the next generation, you could potentially work out how to stop that from happening, but we need much more information.

“That’s one great strength of the Florey – basic neuroscientists interact regularly with clinical neuroscientists and their data, and clinicians receive new information from us about disease mechanisms, to ultimately understand and develop treatments for brain disorders.”

New tools in gene sequencing have allowed advances in epigenetics. But while there is now greater precision in studying genomes, researchers are seeking better ways to collect data on environmental factors.

“One of the revolutions that we’ve been contributing data to is the fact that exposures to environmental factors can affect the epigenetics in sperm and lead to changes in the offspring,” Anthony says.

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Professor Anthony Hannan

“This factor is what I call the ‘envirome’ – the total of environmental exposures from conception through to old age.

“Our work ... shows that we also need to understand and integrate enviromes preconception with data across multiple generations.

“We’re only at the start of being able to collect data quantitatively in ways in which we can start to understand human populations and how individual genomes and enviromes interact.”

Transgenerational epigenetics is exciting medical researchers interested in its potential for human medicine while, simultaneously, capturing the public’s attention at a time when there is intense interest in DNA, genetics and inheritance.

Complementing the epigenetics work, Anthony’s lab is looking at the power of environmental enrichment and how it affects the health of individuals and their offspring.

A cognitively stimulating world, combined with physical activity, changes the brain, behaviour and cognition in the long term. The researchers are trying to understand what happens when epigenetic changes are made to specific genes in particular neurons.

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Professor Anthony Hannan
This image of the brain’s nerve fibre tracts was generated using a new mathematical technique that produces more accurate brain images without requiring costly and time-consuming new scans. Dr Thijs Dhollander, a talented young researcher from Belgium, and Professor Alan Connelly, head of the Florey’s Imaging Division, developed the technique. Their new analysis allows more information to be extracted from magnetic resonance (MR) images, improving the distinction between the brain’s white matter (nerve bundles), grey matter (brain cells) and ventricles (fluid-filled spaces).

The technique will allow Florey researchers to revisit previously acquired scans, adding immense value to existing patient data that can be reanalysed to produce gold-standard images with the highest detail. Importantly, the technique also means new data is still acquired during a standard 10-minute scan, meaning experimental protocols are patient-friendly and cost-effective.

In the clinic, this means Florey’s imaging unit will produce the world’s best images of the location and extent of white matter degeneration across a range of conditions, including Alzheimer’s disease, motor neurone disease and other neurodegenerative conditions.
A creepy but brilliant solution

A few years ago, Professor Steven Petrou was on Queensland’s Stradbroke Island, at a retreat for a group of scientists investigating the use of spider and other venoms to relieve pain.

Steve was talking to colleagues about his work on Dravet Syndrome, a catastrophic form of epilepsy that begins in infancy.

Then came the encounter that would change everything.

The Florey’s deputy director and head of our epilepsy division, was explaining how he and his team were investigating a mutation in a sodium channel, SCN1A. As Steve puts it, this channel is “the little switch that turns a neuron on.”

He uses a car metaphor to explain the concept. There are two types of neurones in the brain: those that act like the accelerator and excite the brain, and others that inhibit the brain, the brake – that gives us healthy brain function.

For someone living with Dravet Syndrome, there is a mutation in the brakes. “In this case, the brakes are broken, and that’s why the disease arises.”

On that day on Stradbroke Island two years ago, there was someone who had the answer.

“We asked the question, can we find a compound, a drug or anything that makes the brake that’s left work harder – a simple concept really,” Steve says.

The University of Queensland’s Professor Glenn King, whose specialty is venomics, was part of that discussion. “Ah,” he said. “We’ve got one.”

Steve recalls the moment, as “just like a bang. It’s happenstance; it came together.”

The encounter, he says, was further evidence in support of a favoured saying by Florey director Professor Geoffrey Donnan that “science is a contact sport”.

Suddenly Steve had access to venomics research teams who were working with the chemistry of venoms from arthropod predators – think spiders, scorpions and centipedes – to develop novel pharmaceuticals to treat chronic pain, epilepsy and stroke.

Venoms are a great source of biologically active substances. A 100 million years or so of evolution has fine-tuned venom peptides into potent agents that can be developed as repurposed medicines for people.

They explored whether a spider’s venom could be useful in the treatment of pain. “I said, ‘Hang on, I’m not interested in treating pain. But I have a disorder here where there’s not enough SCN1A.”

The next step was testing to see how a neuron would behave, on a mouse modelled on a human with Dravet syndrome.

The researchers looked to see how neurones fired when the peptide from the venom was introduced.

Just like when a car’s brakes fail to work, the faulty neuron didn’t kick in as an inhibitor when required. “It couldn’t sustain its activity, and more importantly, it couldn’t sustain it when we really depended on it.”

Picking up another metaphor, the team compared the problem to two light switches being turned on and off quickly. The result would be a bright flash. But with the mutation causing just one light to work, Steve wondered whether it was possible to keep the light on longer.

“It’s not as bright, but there was as much light coming out over a slightly longer period. But was that the same as two going on? That was our concern.”

The result was a resounding yes.

“We gave this drug to one of these neurones and it looked exactly like a normal one,” Steve says. “I looked at it and thought, ‘Oh my goodness, that’s amazing’.”

The potential treatment that could flow from this research fits into the category of targeted therapy. With epilepsy, there are drugs to deal with seizures – the final stage of the affliction.

“If you had a car that crashed into walls all the time because the brakes didn’t work, you might start to build bigger bumper bars.”

“But in the end, what you need to do is tighten the brake lining. That’s what we’re doing – intervening before the seizure with targeted therapy.”

In the case of Dravet Syndrome, it is about finding a treatment for what is a particular devastating affliction, with associated health conditions such as developmental delays.

“It’s absolutely catastrophic and there’s nothing you can do for these kids,” he says.

Steve believes there is “still a bit of the journey to go” in developing the treatment, to determine how to deliver a drug and to work out how stable it will be in the brain.

There is also the prospect that instead of using the peptide from the spider’s venom, a chemical analogue could be developed which is smaller, cheaper and has more favourable properties as a drug.

He hopes government funding will help to develop a treatment that commercial researchers would ignore due to the smaller number of patients involved.

“Let’s say this works. A little pill or an injection that helps these kids with Dravet syndrome.

“Tick that one off. And eventually we’re going to tick off all the genetic human disorders, one by one.”

“It costs money but if you conquer it now, you don’t need to spend money in future on care and long-term support. You can spend the precious health dollar on something else.”

“Turning an idea into a treatment is a difficult and expensive process but I really hope to be there for the whole journey.”

It costs money but if you conquer it now, you don’t need to spend money in future on care and long-term support.

You can spend the precious health dollar on something else.
It was 15 December last year when Margaret Niddrie asked her husband, Stan, a question. He didn’t respond. She was alarmed to see his mouth had dropped on one side and knew immediately her husband had suffered a stroke. She swung into action, called 000, and watched as Stan was admitted to Latrobe Regional Hospital, unable to talk or move the right side of his body.

In Melbourne, with the treatment administered quickly you recover and go home. In country Victoria you had limited options and could end up in a nursing home,” says Chris. "If she hadn’t been treated by telemedicine, she quite possibly would have died in Traralgon.”

"When we started, acute stroke telemedicine wasn’t even a blip in the health department – no one was looking at it, no one understood it," says Chris. "We ploughed on and are now the leading acute stroke telemed program in Australia. We’ve gone from one hospital in Bendigo to 10 in a very short period of time.”

"These doctors drop everything to concentrate 100 per cent on the needs of the patient," Chris says. By early February, more than 450 consultations for suspected stroke had been conducted through the program. Some 91 patients were recommended to receive thrombolysis and 100 per cent on the needs of the patient," Chris says. By early February, more than 450 consultations for suspected stroke had been conducted through the program. Some 91 patients were recommended to receive thrombolysis and, in some cases, the patient being transferred to the Royal Melbourne Hospital by helicopter, plane or ambulance for endovascular surgery to remove a blood clot blocking an artery of the brain. This new and game-changing surgery removes a clot in the brain using a stent.

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As a young student, I learned that psychiatric disorders such as schizophrenia and depression are chronic, severely debilitating illnesses. This inspired me to learn more, and 15 years later, I am still passionate about understanding these complex mental disorders. I want to identify their underlying molecular mechanisms in the hope that one day my research will lead to targeted treatments and ultimately, a cure. I want to understand the role of sex hormones, particularly oestrogen, as sex differences are significant in psychiatric disorders. If oestrogen protects against the development and severity of schizophrenia it has therapeutic potential, an exciting prospect given the urgent need to develop more effective treatments.

Dr Andrea Gogos
NHMRC R.D. Wright Fellow
Head, Hormones in Psychiatry Laboratory

Flory scientists have helped develop a unique device to be implanted next to the brain’s motor cortex – without the need for major brain surgery. The device, a stent-based electrode known as a stentrode, could one day help paralysed people move their limbs. People with spinal cord injuries would use thought to wirelessly control their bionic limbs, wheelchairs, computers or when walking in powered body armour, known as an exoskeleton.

The stentrode, about the length of a matchstick, will be implanted in a blood vessel that sits over the brain. It will record high-quality signals emitted from the motor cortex, and will turn these signals into electrical commands.

The work, a major collaboration between the Florey, the Royal Melbourne Hospital and 16 collaborative institutions, was published in February in the journal, Nature Biotechnology. The initial idea for the breakthrough device came from Royal Melbourne Hospital neurologist, Dr Tom Oxley, a Research Fellow at the Florey and the University of Melbourne. Dr Oxley is interested in vascular systems and electrophysiology and has worked with senior Florey researcher Professor Clive May since 2011.

“It came to me with this idea of creating a device which could be implanted in a blood vessel via the jugular vein,” says Prof May, head of the neurocardiovascular lab. “It was one of those brilliant moments when you realise a great young mind has come up with something quite unique.

“I realised we had to support the project and make it work.”

Major funding from the US Defense Advanced Research Projects Agency, and Australia’s National Health and Medical Research Council followed. Dr Oxley then involved 39 great minds from 16 groups to develop the device with a vascular bionics catheter lab set-up at the Florey.

Fast-forward four years and the device is ready to be tested in humans. It is expected that three candidates will be chosen from a specific patient cohort in 2017. The surgery will take place at the Royal Melbourne Hospital.

Stroke and spinal cord injuries are leading causes of disability, affecting 1 in 50 people. There are 25,000 Australians with spinal cord injuries, with the typical patient a 19-year-old male. About 150,000 Australians are left severely disabled after stroke.

The device has applications far beyond assisting those with paralysis. The stentrode could be used to record brain waves for people living with epilepsy; helping them predict when they are about to have a seizure. People living with movement disorders like Parkinson’s disease, multiple sclerosis or motor neurone disease may also benefit in years to come.

**THE PROJECT**
A bionic implant translating brain signals into messages for artificial limbs.

**THE BENEFICIARIES**
People with spinal injuries.

**THE TALENT**
The Florey’s Professor Clive May and a team of 39 researchers from 16 organisations.

**SEEKING NEW POWER OF THOUGHT**

“Think about moving your legs.”

**STORY CONTINUES >>**
Quadriplegics in the human trials will be encouraged to ‘learn to walk and stand again’ by sending signals to their exoskeleton, according to fellow inventor, biomedical engineer Dr Nick Opie. “With our device, you’ve essentially connected an electronic limb to the patient’s brain, but they have to learn how to use it.”

Prof May says the device is well tolerated. “In fact, the longer the device is in the blood vessel, the better it seems to work. Unlike other devices of the past, this one is not rejected by the brain and is incorporated into the lining of the blood vessel ensuring long-term viability.”

After it has undergone human testing and is ready for market, it is expected the device will be similar in cost to the cochlear implant — around A$15,000 to A$20,000 and will be ready for commercial use by 2022.

It is also hoped the stentrode will be as important to medicine as the cochlear implant, which was invented in Australia.

Professor Terry O’Brien, head of the Department of Medicine at the Royal Melbourne Hospital said the development of the stentrode has been the “holy grail” for research in bionics.

“To be able to create a device that can record brainwave activity over long periods of time, without damaging the brain is an amazing development in modern medicine,” Professor O’Brien said.

Florey Director and neurologist, Professor Geoffrey Donnan, has welcomed the advance and believes it is a great example of the power of collaboration in the Parkville precinct.

You can read the abstract of the Nature Biotechnology paper on
www.nature.com/nbt/journal/vaop/current/full/nbt.3428.html
RESEARCH BREAKTHROUGH FOR TEEN ADDICTION

"The researchers found they could successfully suppress relapse in both anxiety and cocaine addiction. It was a fantastic result. It could mean less use of drugs in treatment and less therapy."

Dr Jee Hyun Kim

A dolescents are particularly vulnerable to drug addiction but the reasons for this haven’t always been clear. Behavioural neuroscientist Dr Jee Hyun Kim and her team hope their research will soon influence kids at this life-changing time.

An insight into the way adolescents deal with fear and anxiety has triggered new research into cocaine and methamphetamine addiction. The brain has an ‘emotional memory’, Jee explains, and is wired to form connections between things that happen to you and your emotions, whether the fear associated with a traumatic event or the ‘highs’ of drug taking. These form strong connections with the environment in which they were experienced and the people with whom they were shared. Being re-exposed to that environment or anything that reminds you of the original event can trigger a relapse. For a teen, just seeing a friend with whom they’ve shared drugs is enough.

The Developmental Psychobiology team is led by Jee who called on researchers Isabel Zbukvic and Sophia Luikinga to take the work to the next step. They figured out the neural mechanism responsible – differences in the prefrontal cortex in dopamine-signalling. (Dopamine is a chemical that triggers the motivation to do something, including pleasure-seeking, and helps with motor control and focussing attention.) The scientists pushed on to find out why.

In a study using a drug now used to treat schizophrenia, at the same time as exposure therapy, the researchers found they could successfully suppress relapse in both anxiety and cocaine addiction in rats. “It was a fantastic result. It could mean less use of drugs in treatment and less therapy.”

Jee is now forming collaborations with Melbourne Neuropsychiatry Centre to conduct a clinical trial in anxious adolescents. Similar research into methamphetamines, a more popular drug with teenagers and more harmful to them, is continuing.

"When you exercise, starting later in life – in the fifties for example – we can restore cognitive flexibility."

Dr Jee Hyun Kim

Dr Jee Hyun Kim’s research into elderly people and cognitive flexibility – the ability to switch attention between thinking about different concepts simultaneously started with a few simple questions.

Research had shown that exercise and mental stimulation early in life could delay the onset of dementia and other degenerative brain disorders. Jee wanted to find out if exercise could also help cognitive flexibility in old age. Or does the brain, like many older people, become set in its ways? If you’re over 50, overweight and inactive is it too late?

"Neurogenesis only takes place in a few areas in the brain – the places that are responsible for cognitive flexibility. That may be the reason we lose it as we age, because neurogenesis slows down."

"Therapy is hope PR collaboration with Melbourne Neuropsychiatry will take the research from bench to bedside to develop drugs or manipulations to enhance cognitive flexibility.

In the meantime, Jee recommends it’s never too late to start exercising.
FINANCIAL Snapshot

SOURCES OF INCOME – 2015

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ENDOWMENT INVESTMENTS AT DEC 2015

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Visit the Australian Charities and Not-For-Profits Commission for detailed financial records of the Florey’s 2015 year.

In October 2016 we will mark the five-year anniversary of the opening of our magnificent purpose-built facilities in Heidelberg and Parkville. The Florey gratefully acknowledges the support of the Ian Potter Foundation and the Myer Foundation, philanthropists, donors, the Commonwealth Government and the State Government of Victoria for their strong support.

Our new facilities provide a first class environment for the country’s largest neuroscientific workforce.

We are attracting visiting scientists from around the world who are drawn to the expertise, new equipment, buildings and energy generated by this superb environment. Our educational and clinical programs ensure our laboratory and clinical research is translated to patients. State-of-the-art imaging facilities, including a powerful 7-Tesla MRI, ensure we recruit people for large clinical trials, influencing global health through population studies.

The buildings are five-green-star energy rated, ensuring we minimise ongoing costs and lighten our environmental footprint.

Florey scientists continue to appreciate the passionate support offered by funders to help them in their quest to improve lives through brain research.
The Florey Institute of Neuroscience and Mental Health is one of the largest brain research centres in the world and the biggest in Australia. Our scientists share a common goal – to improve people’s lives through brain research and, ultimately, to influence global wellbeing and health economics.

Neuroscience is an area of medical research attracting enormous attention as our understanding of the brain rapidly evolves. Internationally, populations are ageing and there is a sense of urgency to find causes, treatments and cures for conditions affecting the brain and mind. We are addressing these conditions to avoid suffering and to contain health-related expenditure.

The Florey is a world-leader in imaging technology, genetics, stroke rehabilitation and epidemiological studies. Mental health research is a growing focus with psychotic illnesses and neurodegenerative diseases demanding attention.

We study:

— Addiction  
— Alzheimer’s disease  
— Autism  
— Cardiovascular disease  
— Mental illness including Anxiety, Schizophrenia, Bipolar disorder and Major depression  
— Epilepsy  
— Huntington’s disease  
— Motor neurone disease  
— Multiple sclerosis  
— Parkinson’s disease  
— Stroke  
— Sudden infant death syndrome  
— Traumatic brain and spinal cord injury

To keep up to date with Florey events, news and research, visit florey.edu.au or email: info@florey.edu.au