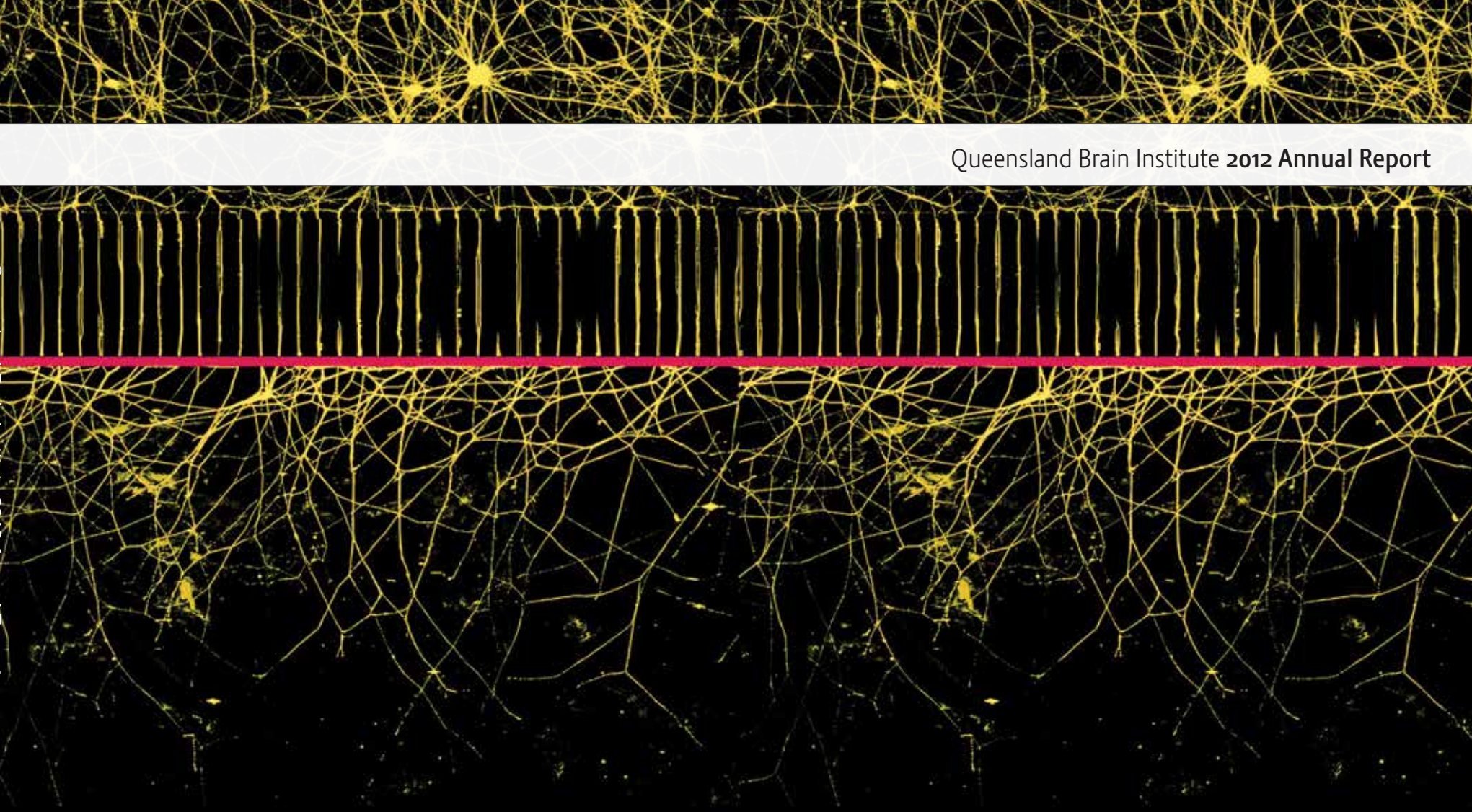

Queensland Brain Institute **2012 Annual Report**

The University Of Queensland
AUSTRALIA

qbi
queensland brain institute

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

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Cover Image: Neuronal processes isolated from their cell bodies by microfluidic channels were severed along the red line and allowed to regrow to study mechanisms of regeneration. (Image repeated horizontally)
Image: Andrew Thompson, Senior Research Technician

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UQ PRESIDENT AND VICE-CHANCELLOR'S REPORT

2012 marked five years since the opening of the purpose-built $63 million facility that houses the Queensland Brain Institute (QBI) at The University of Queensland (UQ).

In these five years QBI has significantly increased the number of scientific staff and students, from 10 students, 18 Principal Investigators (PIs) and 89 staff in 2007, to 92 students, 33 PIs and 350 staff in 2012.

The Institute's success in competitive grant funding has also increased accordingly. Australian Research Council (ARC) support has increased from $2.02 million in 2007 to $5.68 million in 2012, and National Health and Medical Research Council (NHMRC) funding has grown from $2.4 million to $6.63 million over the same period.

Professor Justin Marshall received a prestigious Discovery Outstanding Researcher Award, as part of Australia's largest individual ARC Discovery Project grant. His work investigates the neural processing that underpins the sophisticated forms of colour and polarisation vision exhibited by octopus, squid and mantis shrimps on the Great Barrier Reef.

Further, Dr Oliver Baumann was awarded an ARC Discovery Early Career Researcher Award for his research using neuroimaging techniques to probe the role of the human cerebellum in perceptual processes. This new award identifies research excellence and leadership potential in young investigators, so it is a credit to Oliver to be recognised in this way. His achievements are made more considerable by the fact only 13 per cent of the Award's 2100 applicants were successful.

UQ again received the highest score of 5, or 'well above world standard', in the area of Neurosciences in the 2012 ARC Excellence in Research for Australia (ERA) initiative. This achievement can to a very large extent be attributed to the outstanding work produced by researchers at QBI. A selection of QBI's key findings for 2012 are outlined in the Discoveries section of this report and include fascinating new insights into treating Alzheimer's disease, a mathematical model that underpins brain wiring and work that has brought us closer to developing a therapeutic target for motor neuron disease (MND).

In 2012 internationally renowned neuroscientist Professor Jürgen Götz was recruited as the inaugural Director of QBI's newly established Centre for Ageing Dementia Research (CADR). This Centre brings together research capabilities across the Institute to focus on dementia, one of Australia's most significant health problems, and will be formally launched in early 2013.

QBI Director Professor Perry Bartlett has promoted the Institute's international partnerships. He has strengthened relations with research colleagues in China at the Joint Laboratory of Neuroscience and Cognition with the Chinese Academy of Sciences' Institute of Biophysics in Beijing, and the Joint Sino-Australian Neurogenetics Laboratory with the Changzheng Hospital at the Second Military Medical University in Shanghai. The formal relationship with the Ludwig Maximilians University Munich, Germany, is also gaining momentum with a second symposium planned to strengthen initial collaborations.

In another international success, Queensland student Teresa Tang was named the first Australian winner of the International Brain Bee (IBB) held in Cape Town, South Africa, after initially winning the Australian Brain Bee Challenge (ABBC). The competition for high school students, first established in Australia in 2006 through QBI, is key to developing and encouraging an early interest in neuroscience, and is testament to the Institute's commitment to fostering the neuroscientists of the future. Teresa will complement her IBB win by undertaking a research placement at QBI over the 2012 summer working in Professor Jason Mattingley's Laboratory.

I congratulate Perry and his dedicated team on their tremendous achievements to date, and thank them for helping to cement UQ as a leader in neuroscience research. 2013 is QBI's 10-year anniversary and I look forward to celebrating this notable milestone and all that has been achieved in the past decade.

Professor Peter Høj
President and Vice-Chancellor

QBI DIRECTOR'S REPORT

This year marks an important milestone for our Institute as it is 5 years since we took occupation of our $63 million, purpose-built facility. This world-class facility is home to 33 outstanding research teams and, together with the numerous advanced technologies we have accrued, has allowed us to position ourselves as leaders in neuroscience research in the Asia-Pacific region. Over the past 5 years QBI has enjoyed phenomenal growth, and grant success has been driven by research excellence and productivity.

In what has been a challenging time for state and federal government funding, our research excellence attracted a total of $4.9 million from the National Health and Medical Research Council (NHMRC) to fund ten projects commencing in 2013. Among the recipients was Associate Professor Elizabeth Coulson, who was awarded a grant of $824,640 to conduct a study of sleep disturbance and cholinergic degeneration in Alzheimer's disease. QBI researchers were also awarded $800,000 for new equipment funded under the Australian Research Council's (ARC) Linkage Infrastructure, Equipment and Facilities (LIEF) scheme, $1.125 million in the ARC Discovery Early Career Researcher Awards (DECRAs), and $1.69 million in ARC Discovery Project grants. Included in the recipients of Discovery Project funding was QBI Deputy Director (Research), Professor Pankaj Sah, who was awarded $600,000 to explore how the brain processes, stores and retrieves information.

Our productivity is evidenced not only by an increase in publication numbers – from 62 in 2005 to 210 in 2012 – but also by an increase in the number of publications in the world's foremost journals, with 4 in *Nature*, 1 in *Science*, 2 in *Neuron*, 1 in *Nature Neuroscience* and 7 in *The Journal of Neuroscience*, this year. Among these research achievements was Associate Professor Stephen Williams' unique discovery about how the brain computes sensory information, which was published in the prestigious journal *Nature*, and the development of Professor Geoffrey Goodhill's mathematical model to predict the connections made by nerve fibres during brain development, published in the journal *Neuron*.

This year saw the establishment of the Centre for Ageing Dementia Research (CADR), with the appointment of its inaugural Director, Professor Jürgen Götz, in February. As Australia's first facility focussed entirely on research into the prevention and treatment of dementia – one of the country's most pressing health problems – CADR is quickly attracting the attention of government and the community alike, with significant philanthropic support from the Estate of Dr Clem Jones *AO*, The Helpful Foundation, G James Pty Ltd and the John T Reid Charitable Trusts. Due to the high cost of basic research, QBI is still seeking a total investment of $25 million from government and private donations to drive the Centre. Under the direction of Professor Götz, the CADR team has made significant advances in the area of Alzheimer's disease research. They have discovered that treatment for the disease may lie in modifying the length of subcellular structures responsible for metabolising energy in the brain, the mitochondria. Work within CADR has also highlighted the importance of physical exercise when maintaining a healthy brain. The study, conducted in my laboratory by Dr Daniel Blackmore, found that growth hormone triggers the exercise-dependent activation of stem cells in the adult brain to generate new nerve cells, which reverses the decline in cell number normally observed as animals age. Professor Götz's work is complemented by his remarkable team, which includes NHMRC CJ Martin Fellow, Dr Victor Anggono. The Centre will be formally launched in early 2013.

We have also continued to support the development of our other centres within QBI, including the Science of Learning Centre (SoLC). The SoLC was established with the goal of bringing educationalists and researchers from different disciplines together, in the hopes that we could translate cutting-edge neuroscience into effective, efficient and practical teaching techniques for application in the classroom and workplace. Research from within the SoLC is already helping us to better understand complex neural circuitry, whole-brain activity and the interaction between memory systems, emotion and attention.

I am delighted with the research progress in our joint laboratories with colleagues in China. Work within the Joint Sino-Australian Neurogenetics Laboratory in Shanghai is focussed largely on studying a cohort of nearly 1000 DNA samples from sporadic motor neuron disease (MND) patients as well as 24 familial cases, the outcomes of which will hopefully allow us to identify new genetic markers and ultimately new therapeutic targets for this debilitating disease. The Joint Laboratory of Neuroscience and Cognition in Beijing currently has more than 20 researchers working across five different projects, with a key focus on determining how learning and memory are regulated. There are regular exchanges of scientists, and a joint paper has already been published, hopefully the first of many.

This year we farewelled Ross Maclean Senior Research Fellow, Dr Robyn Wallace, who has played a key role in understanding the genetics of neurological disorders such as MND and epilepsy. In 2012, Dr Wallace continued her impressive work into understanding MND by monitoring the functions of the protein TDP-43 in the nervous system. By understanding the role TDP-43 plays in maintaining connections between nerve and muscle cells and the genes it controls, we can work towards developing therapeutic interventions to delay or eliminate deterioration of the gene. Dr Marie Mangelsdorf has taken over as acting Group Leader and will continue the group's work using advanced genomic techniques to understand how these genes cause MND and to test potential treatments. At the same time, QBI has welcomed the support of the MND and Me Foundation in its quest to improve the understanding of MND. Mr Scott Sullivan, founder of the MND and Me Foundation and an MND sufferer, contributed $70,000 to QBI's research into finding a cure for the disease, which currently affects 1,400 Australians.

Much of our success in garnering community support comes from the committed people around us. I wish to thank our Advisory Board, Dr Sallyanne Atkinson *AO* (Chair), Dr David Merson, Mr Tim Crommelin and Dr Jane Jacobs for their service and support. Equally, I extend my gratitude to our Development Board, Mr Jeff Maclean (Chair), Mr Mike O'Brien, Mr Simon O'Brien, Ms Susan Pearse and Mr Graham McHugh for their commitment to fundraising.

Of course, without the work of our talented staff, none of this would be possible. Thank you to our Faculty, postdoctoral fellows, research assistants, students and support staff. Special mention must go to my Deputy Directors for Research, Professor Pankaj Sah, and Operations, Mr John Kelly, for their unwavering commitment to the Institute. I wish to acknowledge the ongoing support and friendship given by The University of Queensland's Senior Management, in particular Vice-Chancellor, Professor Peter Høj, Senior Deputy Vice-Chancellor, Professor Debbie Terry, and Deputy Vice-Chancellor (Research), Professor Max Lu. I also extend my personal gratitude to our many donors and supporters, particularly in this challenging financial climate. Your support is paramount to the success of the Institute. I look forward to QBI's 10-year anniversary in 2013 and celebrating our many research successes of the past decade.

Professor Perry Bartlett FAA
Director

DISCOVERY

The Queensland Brain Institute

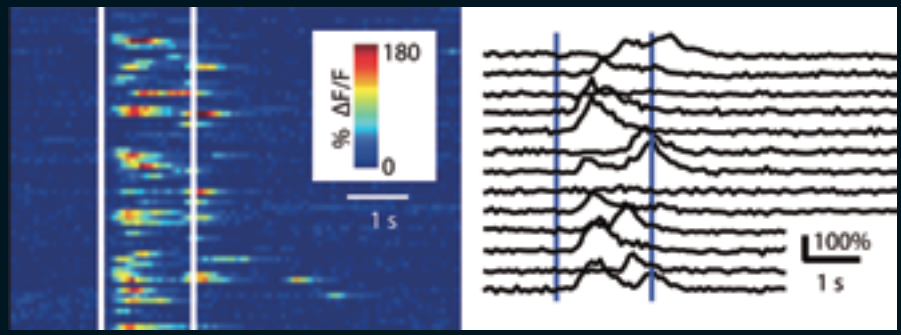
Discovery

In less than a decade, the Queensland Brain Institute has positioned itself as one of the world's leading neuroscience research facilities. Working out of a $63 million state-of-the-art centre, researchers are hand-picked from across the globe along with a host of high calibre students committed to improving the lives and health of Australians.

Research at QBI aims to create an environment of discovery that will ultimately lead to the development of much-needed therapeutic treatments for neurological disorders and neurotrauma.

"By integrating different types of signals such as touch and movement, the brain can perform at lightning speed"

Nonlinear dendritic integration of sensory and motor input during an active sensing task



Researchers from QBI, in partnership with colleagues from the Howard Hughes Medical Institute in the USA, have made a discovery about how neurons process information during behaviour.

Findings of the study, recently published in the prestigious journal *Nature*, show that dendrites – the fine extensions of a neuron, which collect signals from other neurons within a network – operate during behaviour to actively compute the occurrence of sensory and motor signals.

"Our work over the last ten years has shown that active processing occurs in the dendrites of neurons maintained in thin slices of the brain *in vitro*, however, little has been known about the role of dendrites in circuit computations in behaving animals," says Associate Professor Stephen Williams.

These findings will help to better understand how the brain processes multiple types of information to perform complex behaviours.

The researchers used advanced optical imaging and electrophysiological techniques to observe single neurons in the neocortex of behaving mice, during a task where the mice sensed the location of an object using their whiskers.

"In the mouse, one of the major sensory modalities is touch by the whiskers," says Associate Professor Williams.

"We were pleasantly surprised to discover that the dendrites of nerve cells are highly excited during a sensory-motor behaviour," he said.

"More importantly we found that dendritic integration acts to combine motor signals, which control muscle movement, with sensory signals detected from the environment."

By integrating different types of signals such as touch and movement, the brain can perform at lightning speed, allowing animals to predict where a sensory signal occurred in relation to its movement and react accordingly.

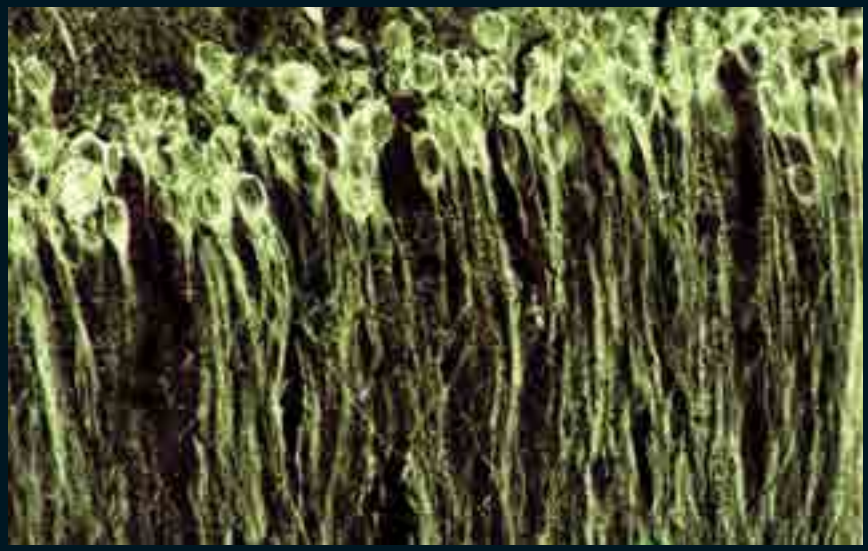
"Whisker movement is triggered by the motor cortex, which sends projections to the distal dendrites of the output neurons in the sensory area of the neocortex.

"When a sensory signal is detected and correlated with motor cortex activity a large output response is generated in the dendrites, which represents the detection of an object in head-centred coordinates," says Associate Professor Williams.

Above: Imaging dendritic activity evoked by active touch. Far left: Associate Professor Stephen Williams.

"The good news is that the development of genetic and drug interventions aimed at reducing mitochondrial length and reversing the toxic effects of TAU can now get underway"

Alzheimer's cure may be a matter of size



Size really does matter according to scientists looking for ways to cure Alzheimer's disease.

Research conducted by QBI and Harvard University has led to the discovery that treatment for Alzheimer's disease may lie in modifying the length of subcellular structures in the brain responsible for metabolising energy, mitochondria.

The study found that in cases where the mitochondria were abnormally long, they induced cell death.

Director of the Centre for Ageing Dementia Research (CADR) at QBI and co-author of the paper, Professor Jürgen Götz, explains:

"Alzhemer's disease belongs to a group of neurodegenerative diseases termed 'TAUopathies', charaterised by clumps of the protein TAU inside neurons.

"In instances where neurons express toxic levels of human TAU, the mitochondria are elongated."

"All cells rely on mitochondria for energy metabolism, and neurons in particular, so controlling the length of these subcellular structures is very important for brain function," says Professor Götz.

The research provides novel targets for therapeutic intervention.

"Treatments currently available for these diseases have at most modest effects, in part due to our limited understanding of how Alzheimer's disease starts and progresses," continues Professor Götz.

The good news is that the development of genetic and drug interventions aimed at reducing mitochondrial length and reversing the toxic effects of TAU can now get underway.

"Aspects of mitochondrial regulation that are being increasingly appreciated are changes in size and shape of the organelle, through a process termed 'mitochondrial dynamics'," says Professor Götz.

Alzheimer's disease affects almost 320,000 Australians. This number is expected to reach over 1 million people by 2050.

Professor Götz, who joined QBI after several successful years undertaking dementia research in Sydney, says the cost of dementia on the economy is immense.

"By the 2060's, spending on dementia is set to outstrip that of any other health condition. It is projected to be $83 billion, and will represent around 11 per cent of the entire health and residential aged care sector spending," he said.

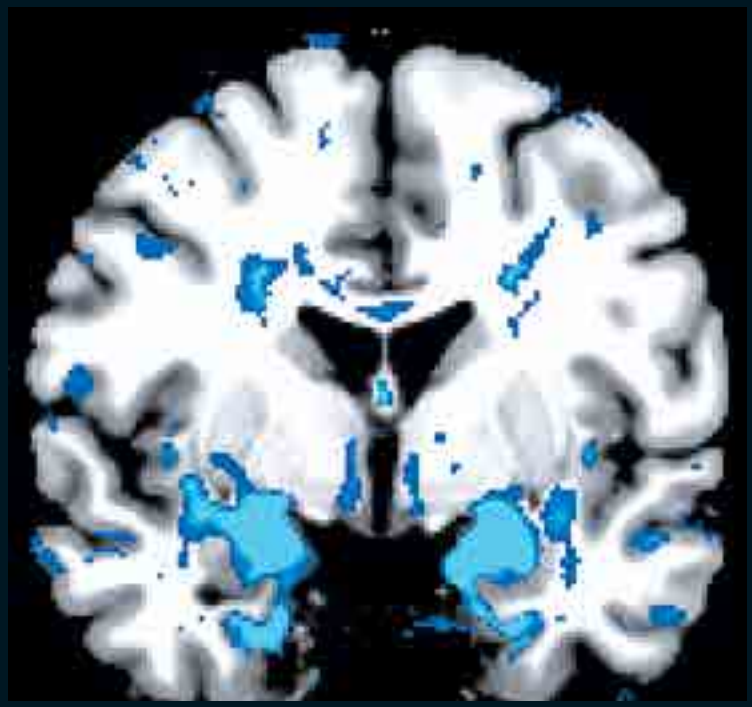
A legitimate research breakthrough that could delay the onset of dementia by 5 years could mean 35.2 per cent fewer cases by 2020 (cumulative savings of $13.5 billion) and 48.5 per cent fewer cases by 2040 (saving $67.5 billion) .

The most common form of dementia is Alzheimer's disease, accounting for around 70 per cent of all cases. Conditions associated with dementia are typically progressive, degenerative and irreversible as there is symptomatic treatment but currently no cure.

Above : TAU aggregates in the hippocampus of a transgenic mouse model of Alzheimer's disease. Far left: Professor Jürgen Götz.

"If this method works in humans it could assist patients to receive the current treatments aimed at reducing the effects of Alzheimer's disease earlier"

MRI gains attention as diagnostic tool for Alzheimer's disease detection



Scientists can now detect early features of Alzheimer's disease using magnetic resonance imaging (MRI) thanks to a study conducted by Associate Professor Elizabeth Coulson.

By analysing MRI scans, Associate Professor Coulson and her team were able to detect loss of basal forebrain cholinergic neurons – an early and key feature of Alzheimer's disease.

"Traditional MRI methods of detecting changes to the brain in Alzheimer's disease require tissue to have undergone significant degeneration such that there is atrophy or loss of the tissue. The aim of this study was to determine whether earlier neurodegenerative changes in the basal forebrain could be detected through MRI using diffusion tensor imaging (DTI), using a rodent model," says Associate Professor Coulson.

"By doing this, we were able to demonstrate that it might be possible to detect signs of Alzheimer's onset, before the basal forebrain cells had actually deteriorated," she said.

The Coulson laboratory are now further developing the methods by analysing human MRI scans.

Detecting degeneration of nerve cells ahead of cell loss gives greater opportunity for targeted intervention.

"If this method works in humans it could assist patients to receive the current treatments aimed at reducing the effects of Alzheimer's earlier and when they are most beneficial," says Associate Professor Coulson.

The current treatments help the basal forebrain neurons to function, but are ineffective if the basal forebrain neurons have already deteriorated.

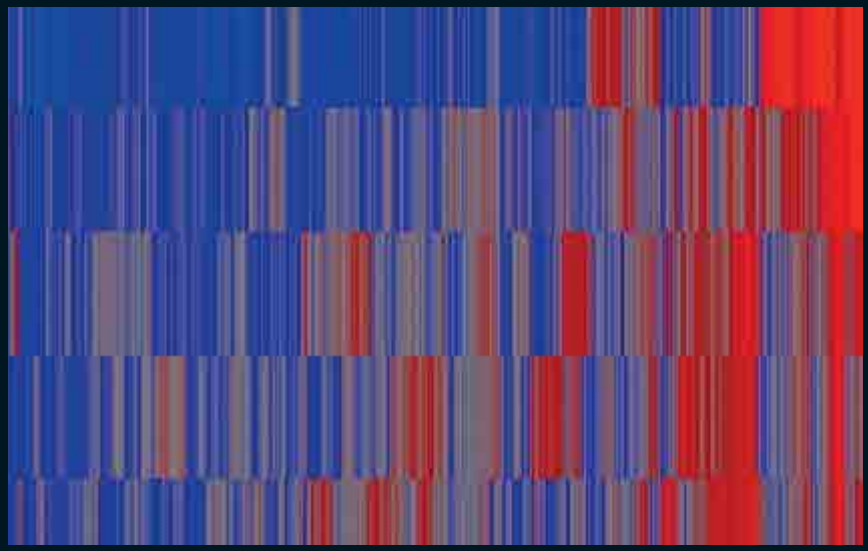
"These findings provide increased support for using DTI and probabilistic tractography as non-invasive tools for diagnosing and/or monitoring the progression of conditions affecting the integrity of the basal forebrain cholinergic system in humans, including Alzheimer's disease."

The project received valuable funding from the Department of Employment, Economic Development and Innovation (DEEDI).

Above: MRI image of a coronal section of a human brain. The areas in blue are those that degenerate early in Alzheimer's disease and include the hippocampus and the basal forebrain. Far left: Associate Professor Elizabeth Coulson.

"QBI's Dr Robyn Wallace says the analysis produced a list of 1,839 potential TDP-43 gene targets"

Scientists clearer on gene linked to motor neuron disease



Researchers at QBI are closer to identifying a therapeutic target for neurodegenerative disorders such as motor neuron disease (MND) after finding a specific protein linked to a number of brain disorders.

The study monitored the functions of TDP-43 in the nervous system, which until now have been largely unknown.

Cytoplasmic inclusions containing TDP-43 are a pathological hallmark of several neurodegenerative disorders, including MND and frontotemporal dementia.

The aim of the study was to identify genes in the central nervous system that are regulated by TDP-43.

An expert in MND and contributor to the study, QBI's Dr Robyn Wallace, says the analysis produced a list of 1,839 potential TDP-43 gene targets, many of which overlap with previous studies.

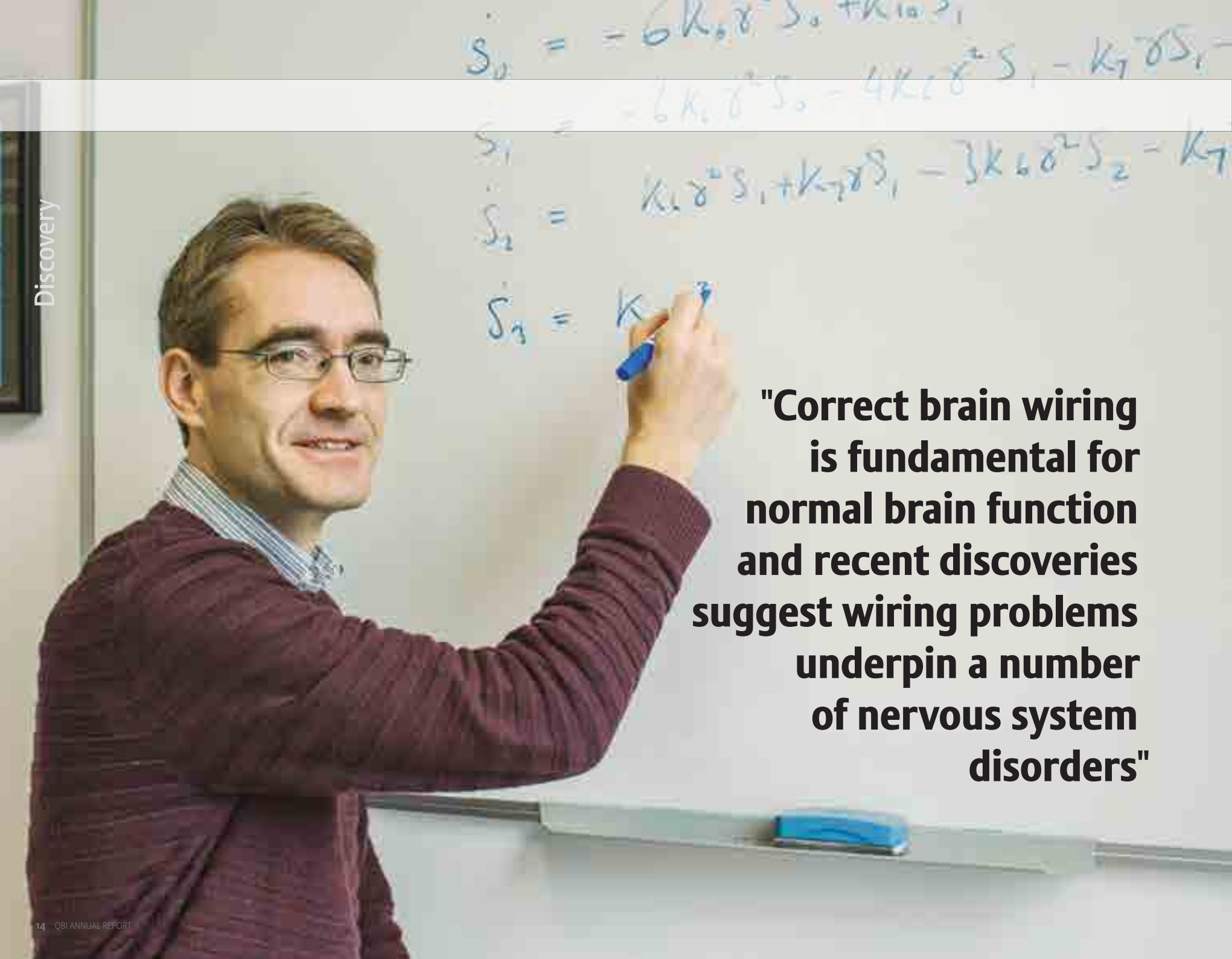
"In the past we have known TDP-43 is an RNA binding protein involved in gene regulation through control of RNA transcription, splicing and transport, however, we haven't been able to precisely pinpoint the genes it controls," says Dr Wallace.

"By understanding the role TDP-43 plays in maintaining connections between nerve and muscle cells and the genes it controls, we can work towards developing therapeutic interventions to delay or eliminate deterioration of the gene."

The findings of the study were published in the journal *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration.*

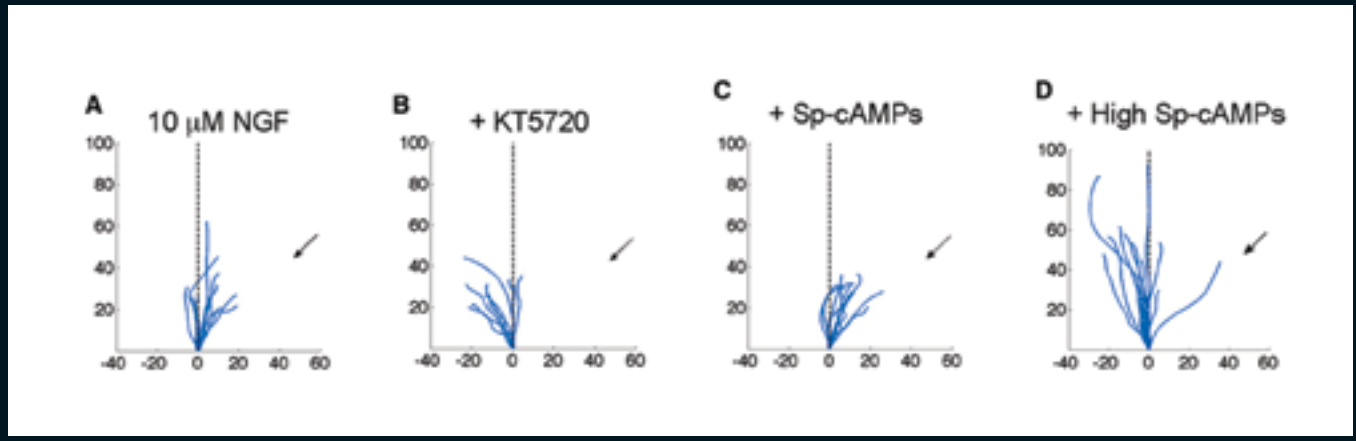
QBI's research into MND is made possible thanks to the Ross Maclean Senior Research Fellowship, the Peter Goodenough Bequest and the MND and Me Foundation.

Above: Hierarchical clustering of RNA binding partners of TDP-43 (TAR DNA binding protein), a splicing regulator in mouse brain using Partek Genomic suite. Far left: PhD student Ramesh Narayanan in the Wallace laboratory.



"Correct brain wiring is fundamental for normal brain function and recent discoveries suggest wiring problems underpin a number of nervous system disorders"

Mathematical model unlocks key to brain wiring



The ability of growing axons to accurately locate targets during development or regeneration is critical for the formation of correct neural circuits.

A new mathematical model designed to predict the directions growing nerve fibres take during brain development may help in the prevention of cognitive disorders.

The model, constructed by an interdisciplinary team of QBI scientists, gives new insight into how changing chemical levels in nerve fibres can modify nerve wiring underpinning crucial connections in the brain.

Professor Geoffrey Goodhill from QBI and UQ's School of Mathematics and Physics says whilst scientists have long known that nerves can be redirected, only now are they understanding why this is the case.

"For a number of decades we've known that the direction of nerve growth can be altered by changing the levels of certain chemicals in the nerve fibre, but we haven't understood why this is the case," says Professor Goodhill.

Correct guidance of axons to their targets depends on an intricate network of signalling molecules in the growth cone.

Calcium and cAMP are two key regulators of whether axons are attracted or repelled by molecular gradients, but how these molecules interact to determine guidance responses remains unclear.

"We constructed a mathematical model for the relevant signalling network, which explained a large range of previous biological data and made predictions for when axons will be attracted or repelled," he said.

"We then confirmed these predictions experimentally, in particular showing that while small increases in cAMP levels promote attraction large increases do not, and that under some circumstances reducing cAMP levels promotes attraction."

Correct brain wiring is fundamental for normal brain function and recent discoveries suggest wiring problems underpin a number of nervous system disorders including autism, dyslexia, Down syndrome, Tourette syndrome and Parkinson's disease.

This model, published in the prestigious journal *Neuron*, demonstrates the important role of mathematics in understanding how the brain works.

Above: The paths taken by neurons in response to a chemical gradient. When the levels of certain chemicals are changed they match the predictions of a mathematical model. Far left: Professor Geoffrey Goodhill.

"The challenge is to find out how to stimulate neuronal production in the aged animal and humans where production has slowed"

Researchers move closer to delaying dementia

QBI scientists are one step closer to developing new therapies for treating dementia following a study aimed at understanding the molecular mechanism that may underlie learning and memory impairment in the ageing population.

"Ageing slows the production of new nerve cells, reducing the brain's ability to form new memories," says postdoctoral researcher Dr Jana Vukovic, who performed the work in the laboratory of QBI Director, Professor Perry Bartlett.

"Our research shows, for the first time, that the brain cells usually responsible for mediating immunity, microglia, have an inhibitory effect on memory during ageing.

"Furthermore, we have shown that a molecule produced by nerve cells, fractalkine, can reverse this process and stimulate stem cells to produce new neurons."

The discovery, published in *The Journal of Neuroscience*, came after the research team observed that the increased production of new neurons in mice that were actively running, was due to the release of fractalkine in the hippocampus – the brain structure responsible for specific types of learning and memory.

Professor Bartlett said it had been known for some time that exercise increased the production of new nerve cells in the hippocampus in young and even aged mice.

"But this study found that it is fractalkine that appears to be specifically mediating this effect by making the microglia produce factors that activate the stem cells that produce new nerve cells," he said.

"Once the cells are activated they divide and produce new cells, which underpin the animal's ability to learn and form memories. This means that fractalkine may form the basis for the development of future therapies.

"The discovery is especially exciting because we have found that older animals suffering cognitive decline showed significantly lower levels of fractalkine.

Dr Vukovic said that until relatively recently, it was thought the adult brain was incapable of generating new neurons.

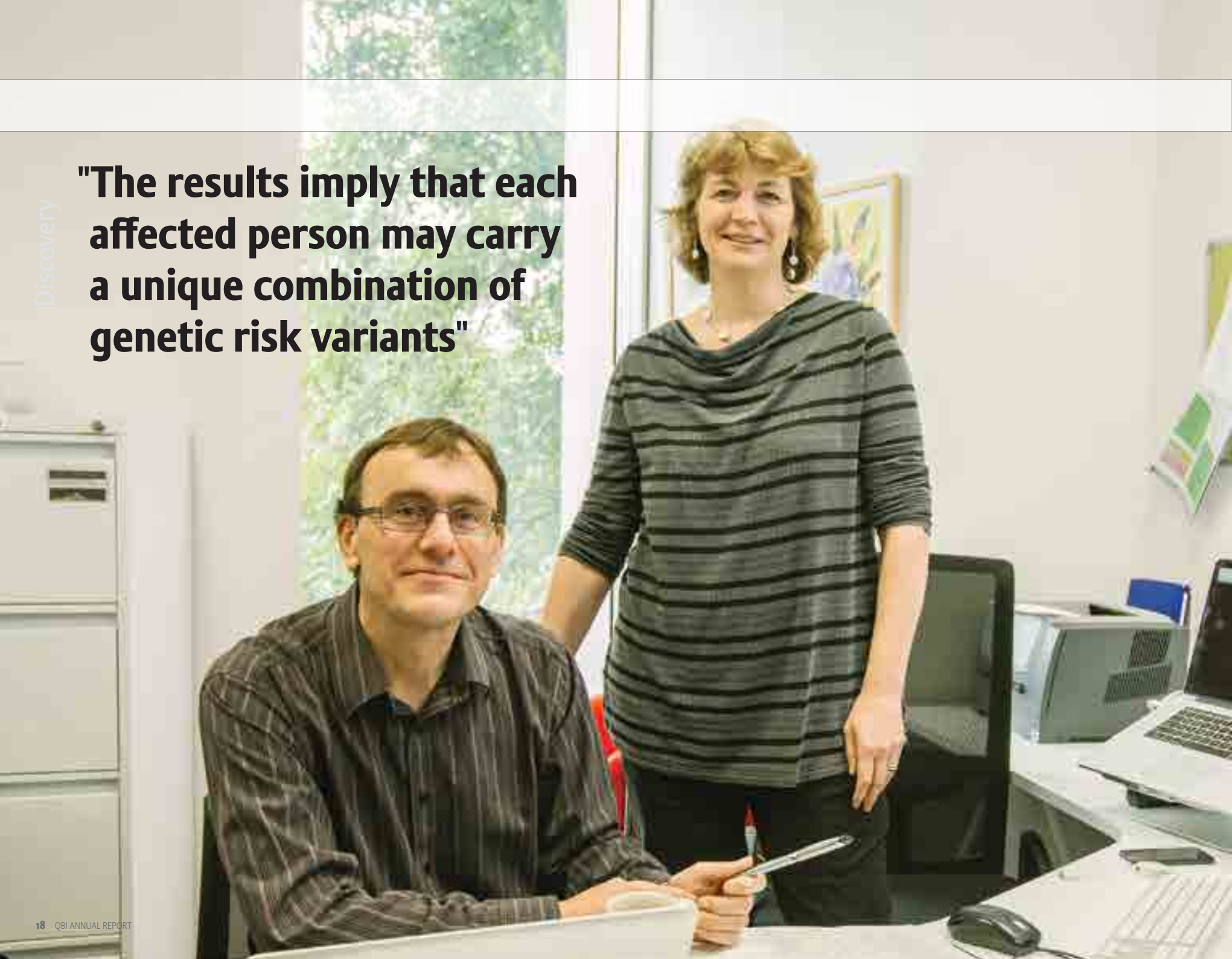
"But work from Professor Bartlett's laboratory over the past 20 years has demonstrated that the brains of adult animals retain the ability to make new nerve cells," she said.

"The challenge is to find out how to stimulate neuronal production in the aged animal and humans where production has slowed."

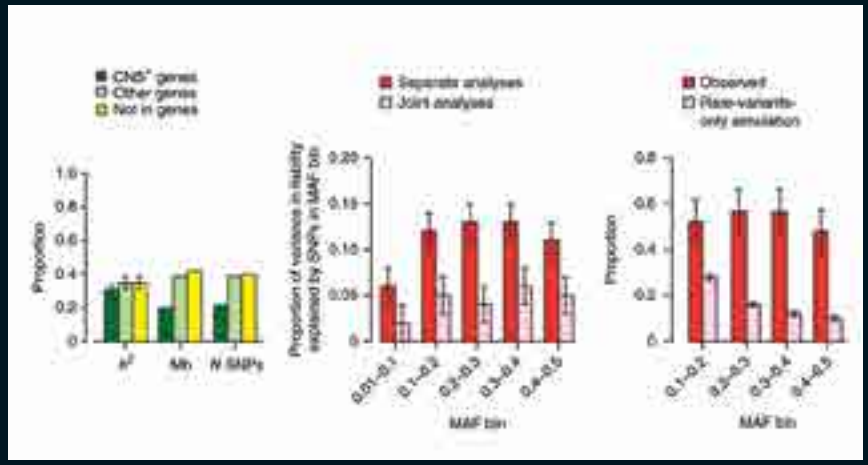
The latest work was a "significant step toward achieving this goal," she said.

Above: In an ageing brain, microglial cells can inhibit activation of neural precursor cells in the hippocampus. Image Jana Vukovic. Far left: Professor Perry Bartlett.

"The results imply that each affected person may carry a unique combination of genetic risk variants"



Novel analysis offers clues to schizophrenia underpinnings



Above: Results from analyses validate that genes preferentially expressed in the brain (CNS+ genes) are overrepresented in their contribution to risk of schizophrenia and that its genetic architecture includes an important contribution from common genetic variants (or SNPs; MAF = minor allele frequency). Left: L-R Professor Peter Visscher and Associate Professor Naomi Wray.

Schizophrenia is a common, chronic and often devastating brain disorder characterised by persistent delusions and hallucinations.

It affects about 1 person in 100 at some point in their lives and usually strikes in late adolescence or early adulthood. Despite the availability of effective treatments, the course of the illness is usually chronic, and response to treatments is often limited, leading to prolonged disability and personal suffering. Family history, which signifies genetic inheritance, is a strong risk factor for schizophrenia.

A new method of genetic analysis developed by researchers based at QBI, the University of Queensland Diamantina Institute (UQDI) and the Queensland Institute of Medical Research (QIMR) has shed new light on the elusive genetic underpinnings of schizophrenia.

While previous studies have pinpointed several genes along with rare chromosomal deletions and duplications associated with the disease, these account for less than three per cent of the risk of schizophrenia.

But the new method found that about a quarter of schizophrenia is captured by many variants that are common in the general population.

According to QBI's Associate Professor Naomi Wray, who co-led the international study together with Professor Peter Visscher, this suggests that we all carry genetic risk variants for schizophrenia, but that the disease only emerges when the burden of variants, in combination with environmental factors, reaches a certain tipping point.

"The results imply that each affected person may carry a unique combination of genetic risk variants, which in turn is consistent with a spectrum of symptoms and treatment responses," says Associate Professor Wray.

Published in *Nature Genetics*, the study uses very distant genetic relationships between individuals that are estimated from nearly a million DNA markers, and shows the extent to which people with schizophrenia have more similar genomic profiles to each other than to people unaffected by this disorder.

This is the largest study of its kind to date with more than 20,000 participants.

QBI's Professor Bryan Mowry contributed one of the largest single site cohorts of over 600 cases to the international consortium.

Professor Visscher says the results hold hope that as even larger study samples are collected, more specific genes will emerge, which will provide clearer insights into the underlying biology of schizophrenia patients.

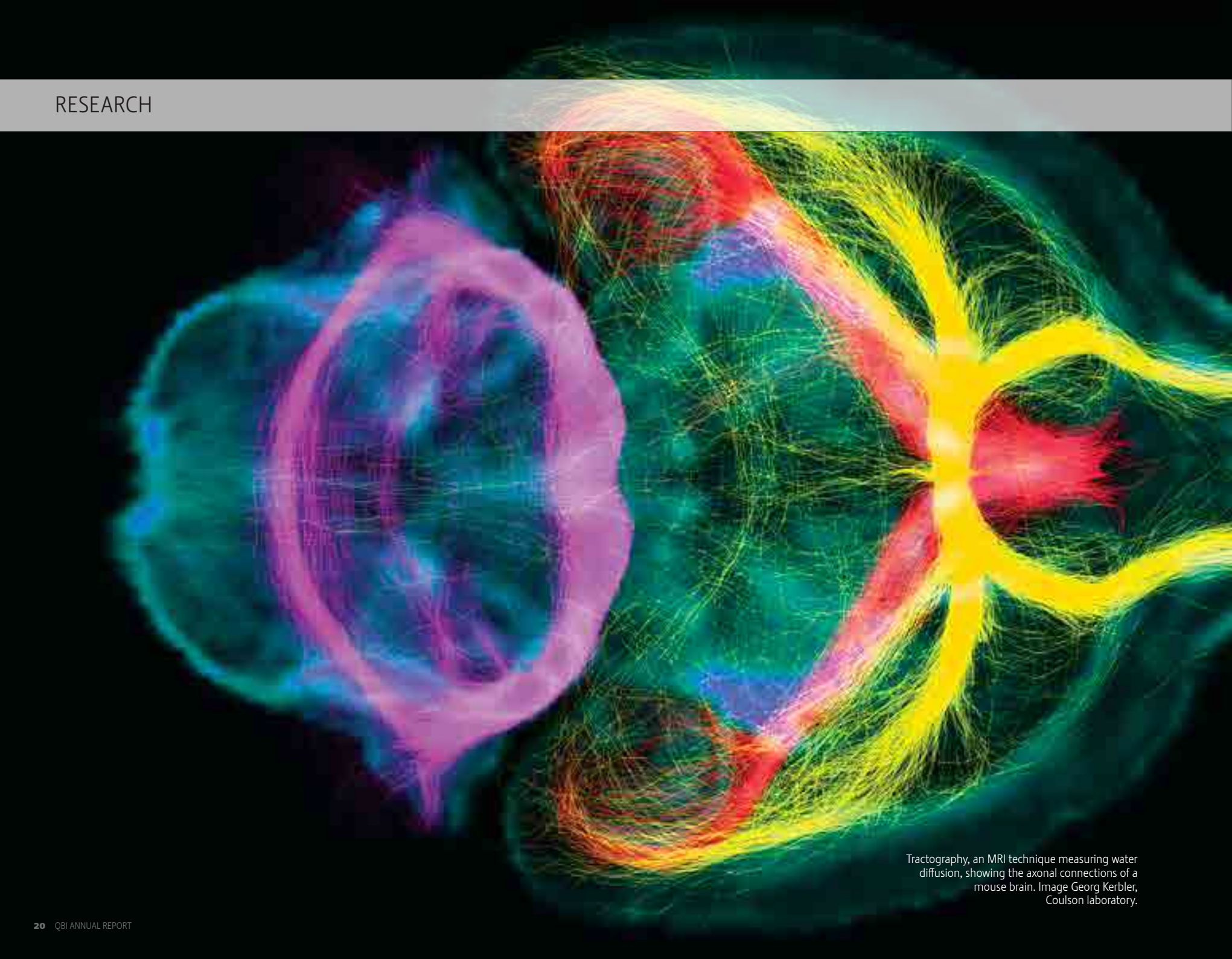
It is a paradigm that has already proven to be successful for other complex genetic traits and disorders, such as Crohn's disease.

Associate Professor Wray says that a better understanding of the genetic architecture of schizophrenia will ultimately aid the earlier diagnosis and management of the disorder.

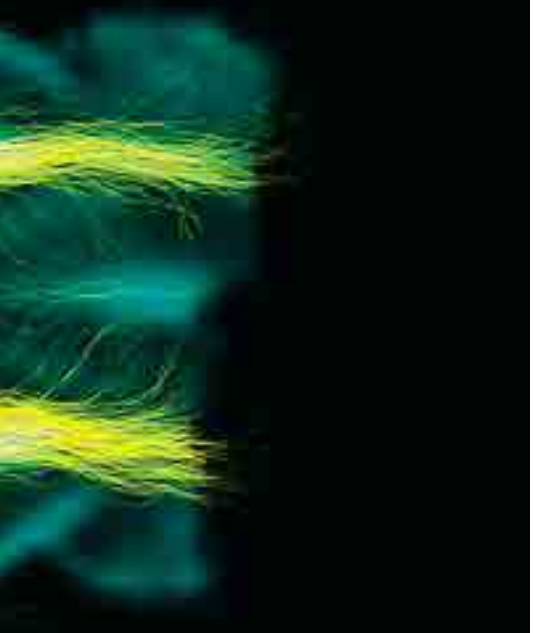
"Because the risk of any one gene is so low, in order to make further progress we need to gather even larger cohorts that are carefully collected with detailed symptom and treatment information," she says.

Associate Professor Wray is one of 96 co-signatories of a letter published in 2012 in *Molecular Psychiatry*, calling for investment in larger cohorts for genetic studies of psychiatric disorders.

"Larger cohorts will allow us to identify biological pathways contributing to risk of schizophrenia and to identify patterns in genomic profiles in different groups of affected people, which is the key to personalising treatments," she says.



Tractography, an MRI technique measuring water diffusion, showing the axonal connections of a mouse brain. Image Georg Kerbler, Coulson laboratory.



Research

The Queensland Brain Institute is a world-leading research facility whose staff are committed to discovering the fundamental mechanisms regulating brain function.

Our findings are applied to the development of new therapeutic approaches to combat diseases in which brain function has failed or is compromised.

QBI's goal is to make a positive impact on the Australian community by helping to reduce the huge social and financial cost of neurological and mental illness.

2012 Laboratory Members L-R: Perry Bartlett, Daniel Blackmore, Lavinia Codd, Dhanisha Jhaveri, Jing Lu, Cornel Mirciov, Estella Newcombe, Boris Prosper, Gregory Robinson, Mark Spanevello, Chanel Taylor, Sophie Tajouri, Jana Vukovic, Jing Zhao. *Not pictured:* Weichuan Mo. **Background:** In an ageing brain these microglial cells can inhibit activation of neural precursor cells in the hippocampus. Image Jana Vukovic.

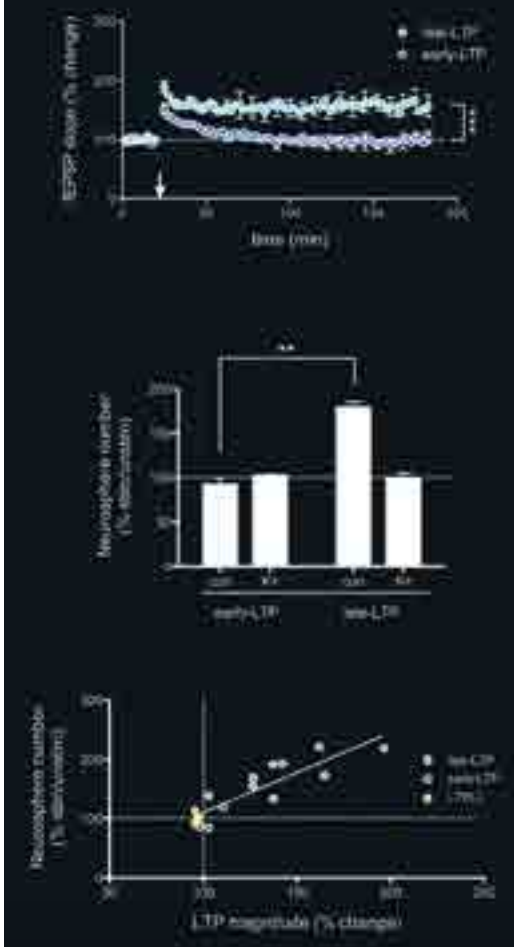
Activating neuronal production in the adult brain

Resident populations of neural stem and precursor cells drive the continuous production of new neurons in a region of the adult brain known to be important in learning and memory - the hippocampus. Recent discoveries from the Bartlett laboratory have highlighted that a large proportion of these precursor cells are in fact quiescent and can be activated to produce new cells. The team is now focussed on identifying the factors that can trigger activation and production of these newborn neurons, and understanding the mechanisms that underlie these processes.

In a study published in *The Journal of Neuroscience,* the group showed that endogenous microglia, the brain's resident immune cells, can exert a dual and opposing effect on neural precursor cell activity within the hippocampus. Exercise has previously been shown to promote neurogenesis in the adult brain and in the 2012 study, the group showed that microglia mediated the increase in neural precursor activity induced by exercise. It demonstrated that even in aged animals exercise induces a positive microglial response.

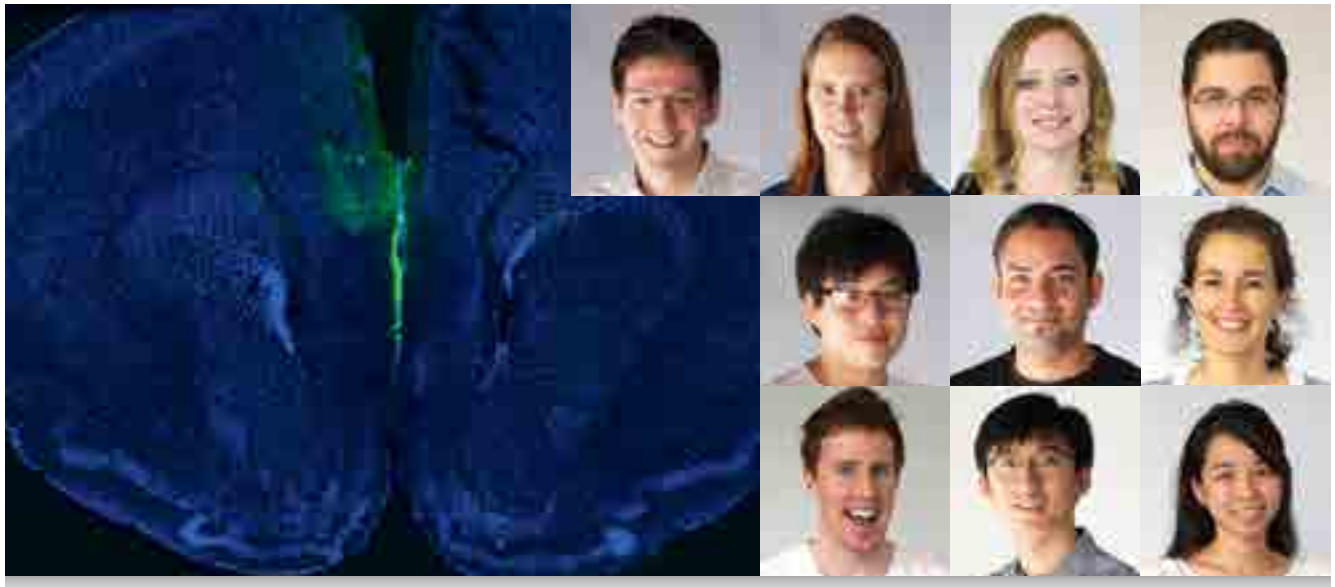
In a study published in *PLoS ONE* the Bartlett group demonstrated that growth hormone mediates precursor cell activation after exercise in the subventricular zone, another neurogenic area of the adult brain. In addition, they found that administering growth hormone directly into the brain of an aged animal triggered precursor cell activation, whereas blocking the effects of growth hormone prevented this activation.

During 2012 the Bartlett laboratory provided direct evidence that patterns of synaptic activity associated with learning and memory can activate quiescent cells in the adult hippocampus. The study, published in *Translational Psychiatry*, showed that the successful induction of long-term potentiation (LTP) results in significant activation of the neural precursor cells and production of new neurons. The results suggest that LTP induction primes hippocampal precursor cells to respond to factors that directly activate proliferation.



The induction of *in vivo* LTP (a form of synaptic strengthening that underlies memory and learning) significantly increases the activation of quiescent neural precursor cells in the mouse hippocampus, thus enabling these cells to start proliferating. Intriguingly, the magnitude of LTP positively correlates with the extent of precursor activation. These results give us insight into how memory and learning processes can stimulate neurogenesis.

Laboratory Head **Dr Timothy Bredy**



2012 Laboratory Members L-R: Timothy Bredy, Danay Baker-Andresen, Charlotte Flavell, Rodrigo Grassi-Oliveira, Xiang Li, Vikram Ratnu, Paola Spadaro, Michael Troup, Wei Wei, Jocelyn Widagdo. *Not pictured:* Bibi Bardril, Elliot Lambert. **Background:** Lentiviral infusion into the prelimbic prefrontal cortex. Blue indicates DAPI, a nuclear marker, and green indicates GFP.

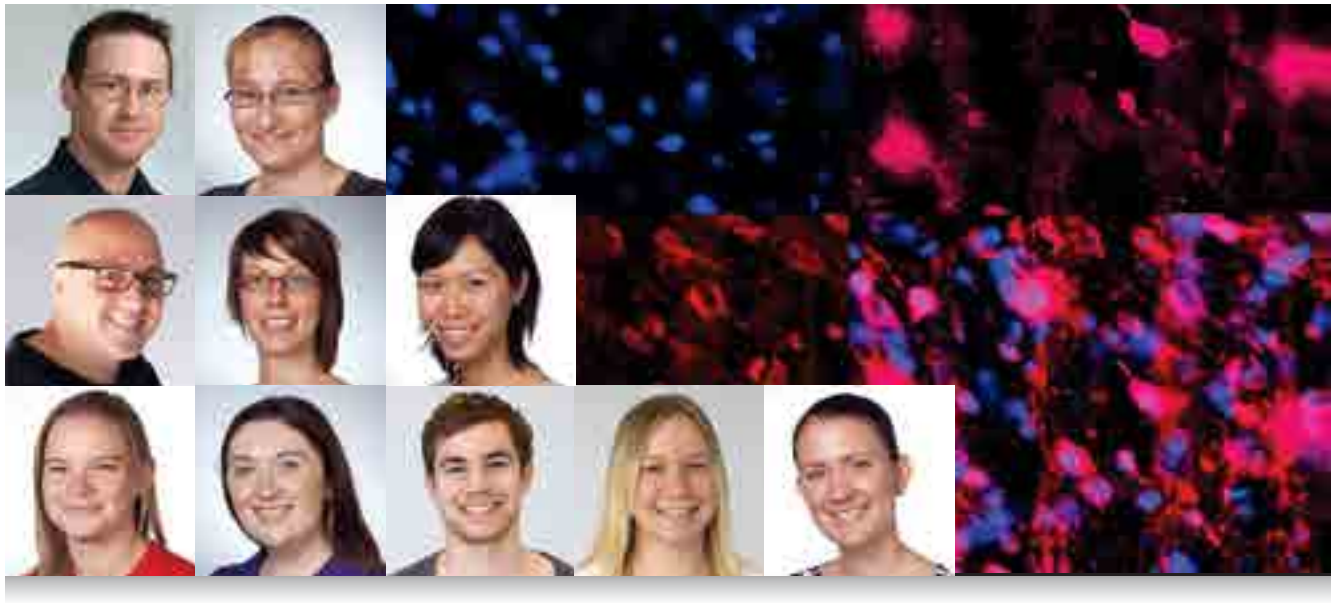
Epigenetic mechanisms regulating memory

The extinction of conditioned fear, the reduction in responding to a feared cue when the cue is repeatedly presented without any adverse consequence, is an important model for the treatment of anxiety disorders. Like other forms of learning, long-lasting memory for fear extinction depends on coordinated gene expression and the synthesis of new synaptic proteins. This process involves a tightly controlled interplay between transcriptional machinery and enzymes that regulate chromatin structure. Research in the Bredy laboratory is elucidating how the genome is connected to the environment, and how this relationship shapes behaviour across the lifespan. The group is particularly interested in how epigenetic mechanisms, including DNA methylation, histone modifications and the activity of non-coding RNAs regulate the formation and maintenance of memory.

2012 was once again a productive year for the laboratory, which published an important review article on non-coding RNAs and neural plasticity in the journal *Frontiers in Genetics*, as well as a major discovery on the role of epigenetic mechanisms in fear extinction. This work, which appeared in *The Journal of Neuroscience,* demonstrated that the histone acetyltransferase p300/CBP-associated factor regulates fear extinction through direct effects on a regulatory transcription factor called ATF4. These findings have significant implications for the development of novel therapeutic approaches for the treatment of fear-related anxiety disorders.

Word cloud describing the group's recent research focus in epigenetics.

Laboratory Head **Dr Thomas Burne**



2012 Laboratory Members L-R: Thomas Burne, Suzanne Alexander, Carlos Coelho, Claire Foldi, Pauline Ko, Natalie Groves, Lauren Harms, Lachlan Harris, Emilia Lefevre, Karly Turner. *Not pictured:* Michelle Sanchez Vega. **Background:** The effect of adult vitamin D deficiency on GABAergic interneurons in the prefrontal cortex of mice.

Using animal models to study brain development and behaviour

Research in the Burne laboratory is focussed on investigating the underlying biological basis for schizophrenia, with the goal of finding public health interventions that will alleviate the burden of this disease. The group has been exploring the impact of developmental vitamin D deficiency on brain development, the impact of adult vitamin D deficiency on brain function and behaviour and, more recently, the neurobiological effects of low dose alcohol exposure during gestation on cognitive behaviour.

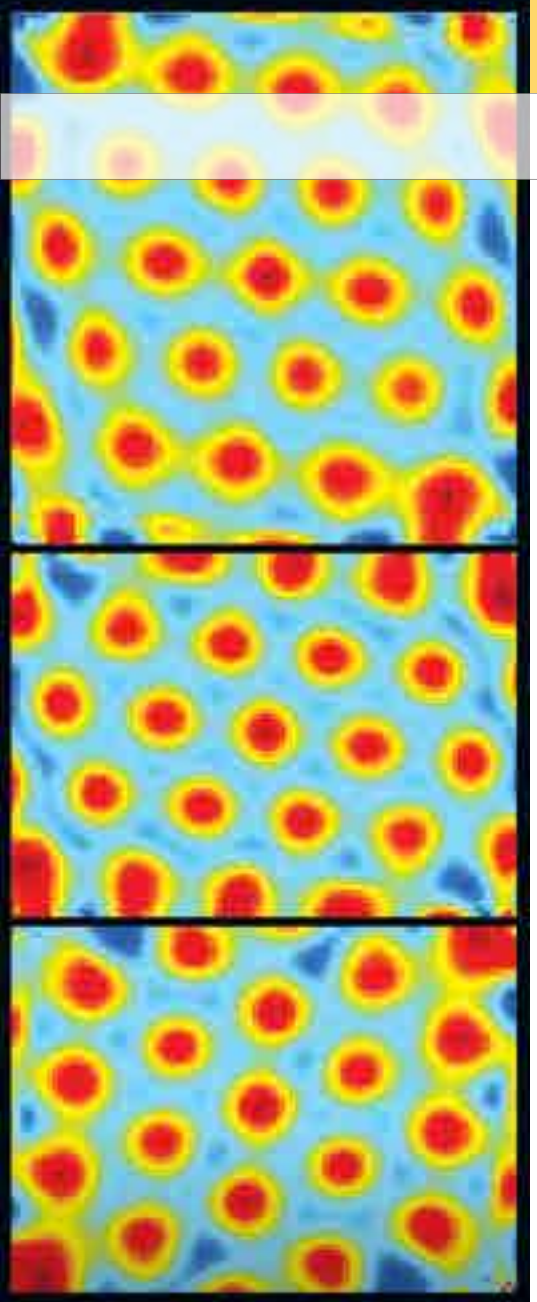
In 2012, the Burne group in collaboration with Associate Professor Darryl Eyles and Professor John McGrath, built on its previous research showing that low prenatal vitamin D (the 'sunshine hormone') is associated with alterations in behaviour, brain neurochemistry and receptor profile associated with vitamin D deficiency in animal models. Ongoing National Health and Medical Research Council funding allowed the group to dissect the exact neural pathways involved in cognitive impairments of attentional processing in developmentally vitamin D deficient rats to model the cognitive symptoms of schizophrenia. The group has now shown that low vitamin D levels during adulthood has an impact on behaviour and brain neurochemistry in rodents. These results provide the first evidence in mice to show that adult vitamin D deficiency impacts on neurotransmitter systems that are affected in a number of neuropsychiatric conditions, including autism, schizophrenia and depression.

Exposure to environmental insults during pregnancy can harm a developing foetus and have life-long effects on health and well-being. The group has begun to use an animal model of foetal alcohol syndrome to explore the hypothesis that alcohol exposure *in utero* compromises epigenetic silencing leading to genetic and transcriptional variation in the brain and ultimately altered behaviour in adulthood. This work is an ongoing collaboration with Dr Suyinn Chong at the Mater Medical Research Institute.

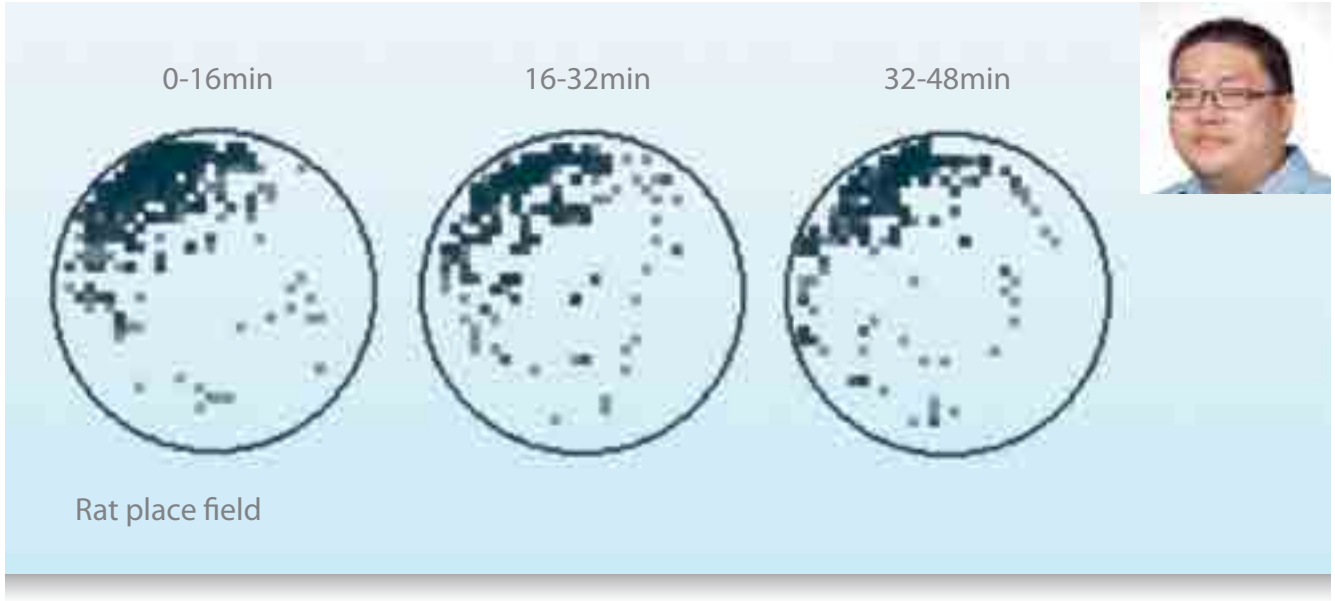
Lauren Harms preparing prefrontal cortex samples for analysis.

Dr Thomas Burne holds a conjoint appointment with Queensland Health.

Laboratory Head **Dr Allen Cheung**



Grid field autocorrelogram predictions based on a cognitive map model, showing partial grid deformations reminiscent of partial grid field rescaling found in rats when vision is used.



2012 Laboratory Members: Allen Cheung. *Not pictured:* Zóltan Kósci (based at Australian National University). **Background:** Modelling the rodent navigation system in the absence of vision. A rat's hippocampal place cells fire stably in darkness yet its head direction system drifts in the first two minutes.

Understanding the brain computations needed for spatial navigation

The core research of Dr Cheung's laboratory is aimed at understanding the fundamental brain computations required for spatial navigation. Spatial navigation is one of the oldest and most widespread brain functions in the animal kingdom. The cells, circuits and computations required for animals to search for resources, return home, and go back to those resources later, are subjects of intense research worldwide.

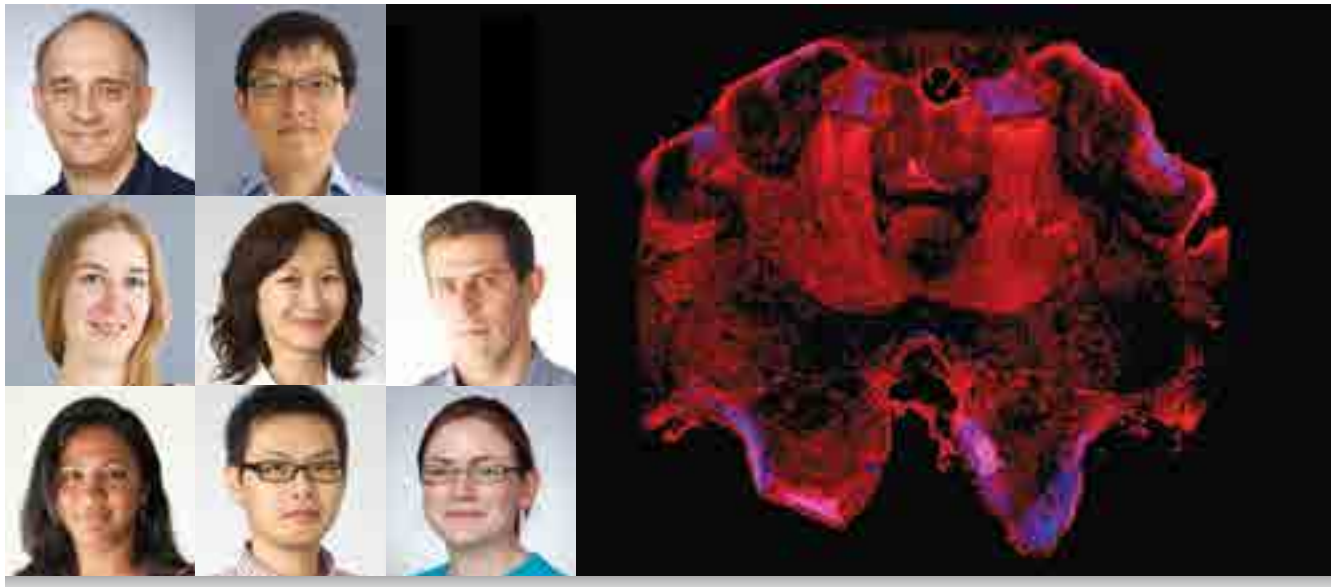
Path integration is one strategy used by vertebrates and invertebrates alike, and may well be the common 'scaffold' required for spatial navigation. It is the process whereby estimated self-motion is integrated over time to yield an approximate vector between the starting location and current location. This form of navigation is prone to noise, which leads to errors in navigation.

A number of laboratories have shown that rats have neurons (place cells and grid cells) that 'know' where they are in total darkness. These contrast with the rapid build up of 'drift' errors reported in the head direction cells under similar conditions. Dr Cheung recently resolved this conflict by the theoretical demonstration that it is necessary to combine arena boundary information with path integration. Implications for the neural networks involved in such computations are now being investigated through theoretical modelling and computer simulations.

In a recent collaboration with Professor Pankaj Sah's laboratory, *in vivo* recordings were performed in the brains of freely moving rats. A digital wireless system was used to record the spikes from individual neurons in the rat's hippocampus, while the animal foraged in a large outdoor arena. Recently, place fields have been identified using this system. Exciting opportunities and challenges lie ahead to develop the experimental and theoretical tools to study the rodent brain in larger, more naturalistic environments.

Research from the Cheung laboratory was published in *PLoS Computational Biology* and *PLoS ONE* in 2012.

Laboratory Head **Associate Professor Charles Claudianos**



2012 Laboratory Members L-R: Charles Claudianos, Joon-Yong An, Stephanie Biergans, Ming-Yu Chen, Alexandre Cristino, Nivetha Gunasekaran, Shao-Chang Huang, Aoife Larkin. *Not pictured:* Flavia Freitas. **Background:** Shown is immunostaining of neuroligin 2 (red) and overlapping RNA expression of embedded miR-932, associated with learning and memory integration regions (mushroom bodies) of the bee brain. DNA staining of cell bodies is shown in blue.

Synapse development and cognitive disorder

The major aim of the Claudianos laboratory is to characterise key molecular processes involved in synapse development that provide detailed insight into the aetiology and diagnosis of cognitive disorder. Many data now show that a loss of synapses or aberrant synaptic connection between neurons will affect brain function. Molecules involved in synapse development such as neurexin and neuroligin now head a list of causative molecular associations in the pathogenesis of autism spectrum disorders (ASDs).

Using tractable insect genetic and behavioural models, the fly and the honeybee, the laboratory examines the role of these molecules and their fundamental biological relevance to healthy brain function. The Claudianos group, in collaboration with QBI colleagues, has demonstrated that the small animal brain can be a useful tool for researching the biological basis of genes that contribute to neurodevelopmental and neuropsychiatric disorders. This work was recently published in the journal *Molecular Psychiatry*. Small animal model validation of candidate disorder genes is then incorporated into an analysis of the human genome. We use systems biology and complex network approaches to identify interactions and regulation of candidate disorder genes to help define key processes and pathways in which these and other candidate ASD, schizophrenia, attention deficit hyperactivity disorder and X-linked intellectual disability genes are involved. This systems approach has helped us abstract a molecular basis for human mental health disorders and provides a 'genetic hypothesis' to assess genetic screening data from affected individuals.

During 2012 the Claudianos laboratory, together with collaborators from the University of Western Australia and the Telethon Institute, completed the first whole genome sequence (exome) analysis of Australian autism families.

Shown is a hypothetical network of 4000 genes associated with mental health disorders. Degree of connection between candidate disorder genes: ASD (blue), X-linked intellectual disability (red), attention deficit hyperactivity disorder (yellow), schizophrenia (green), including comorbid genes (magenta) and indicated by coloured circles.

Laboratory Head **Dr Robert Colvin**

2012 Laboratory Member: Robert Colvin. **Background:** Our understanding of the interplay between attention and memory processes will help us design interactive educational tools.

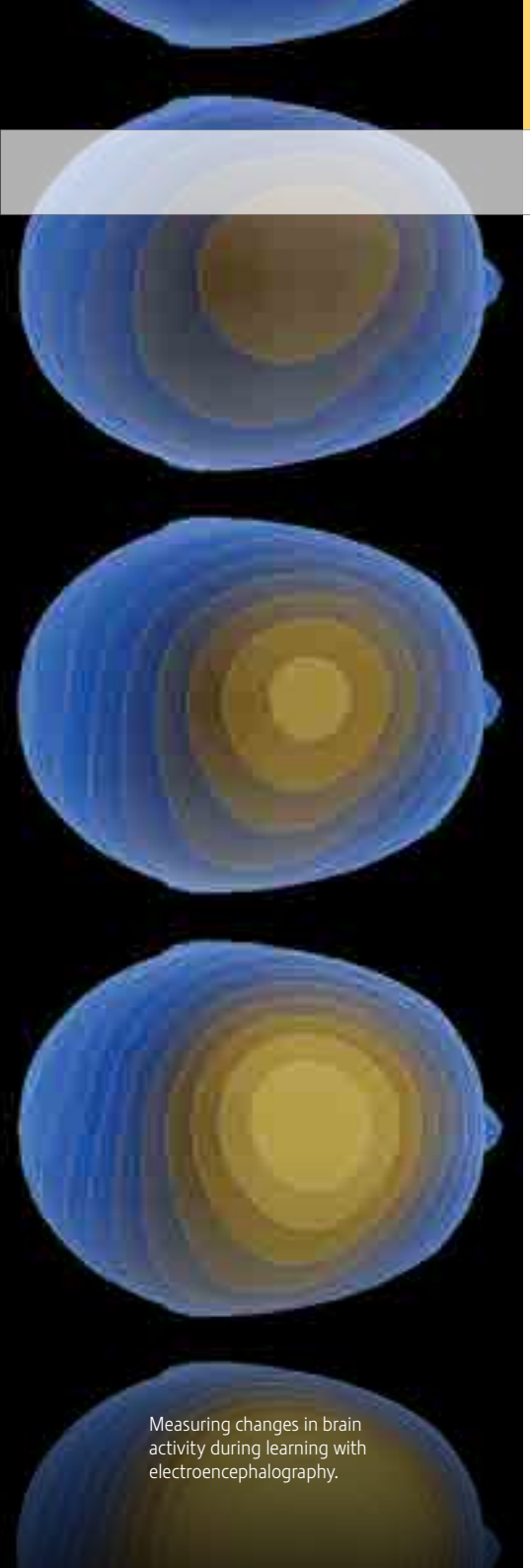
Uniting brain biology and learning behaviour

A major challenge facing research into learning in real environments is the unification of what we know about the biology of the brain with the behaviour exhibited while learning. Cognitive behaviour can be understood at three key levels: the outcomes of specific behaviour in the real world; the general cognitive processes used, such as working memory, attention, and pattern recognition; and the real-time interaction of billions of neurons within the brain. Traditionally the three levels are approached separately, leading to a limitation on the explanatory power of the results.

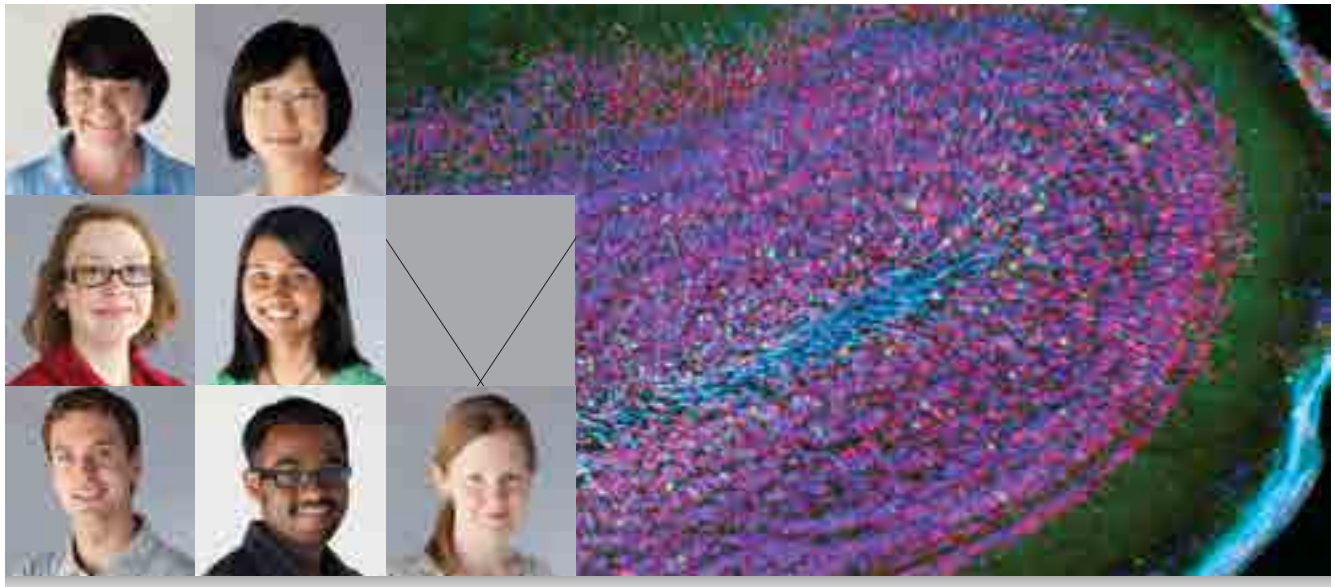
In 2012, a common modelling framework was developed that allows seamless description of chemical properties of neurons alongside more familiar "real-world" behaviour. This framework is built on formal foundations from mathematical logic, allowing simulations and proofs of the relationships between the different levels. The framework is now being applied to understanding the learning of temporal associations, as a precursor to more complex reasoning tasks.

The Colvin laboratory, in collaboration with the Mattingley group, established improved learning outcomes for a difficult logical task under interleaved practice, a result that has until now been shown only for relatively simple memory tasks. Interleaved practice involves the practice of multiple topics in the same block, rather than each being studied in isolation. The goal is to understand how this somewhat unintuitive result at the behavioural level is manifested in and supported by our neural mechanisms of attention and memory.

In a related project conducted in collaboration with the Cunnington and van Swinderen groups, visual attention was found to decrease as proficiency was gained in a simple computer-based task. This provides an insight into how our brain processes visual information and practice and converts it into performance improvements.



Measuring changes in brain activity during learning with electroencephalography.



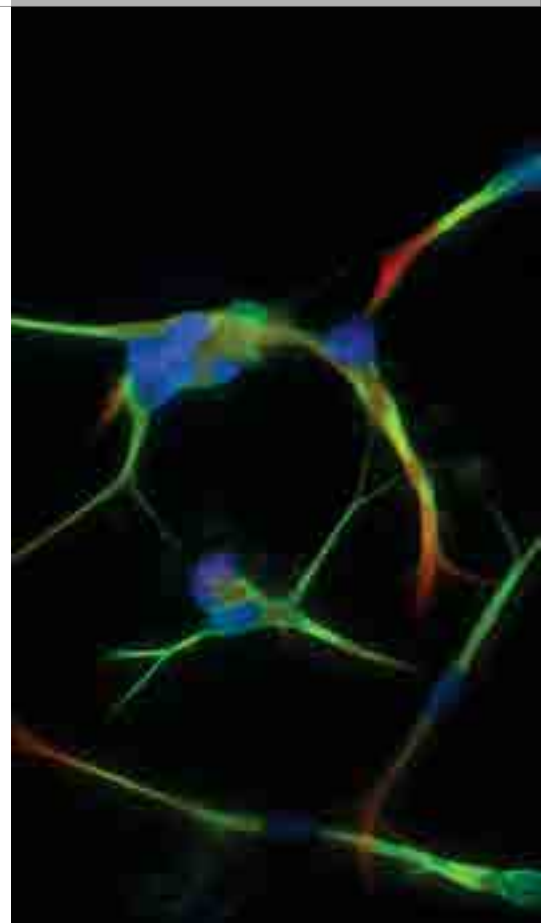
2012 Laboratory Members L-R: Helen Cooper, Min Chen, Charlotte Clark, Jayani Hewage, Casey Holding, Conor O'Leary, Murugesh Sheekar, Amanda White. *Not pictured:* Cathrin Nourse. **Background:** The birth of new neurons: newborn neurons begin to extend their axons and dendrites.

Dissecting the molecular mechanisms regulating the birth of new neurons

The complex architecture of the adult brain is achieved through the tight coordination of neural stem cell activity and neuronal production and integration into the expanding neural networks of the developing nervous system. The goal of the Cooper laboratory is to understand how the local environment of the stem cells and newborn neurons influences neurogenesis. The group has now identified two cell surface receptors that control the birth of new neurons in the embryonic cortex. They have discovered that mutations in neogenin severely disrupt the structure of the stem cell niche, resulting in the formation of cortical malformations similar to those seen in human syndromes. In a second study they have identified the Wnt receptor, Ryk, as a key control point in the decision of newborn cortical neurons to adopt the correct identity – an essential requirement for the development of a fully integrated and functioning neocortex. The group is now mapping the molecular signalling pathways controlled by these receptors in the developing brain. This research is expected to provide invaluable insights into the mechanisms underpinning the aetiology of devastating cortical malformations.

In the adult brain the functional integration of newborn neurons into the established circuitry of the olfactory bulb is essential to the animal's response to environmental stimuli. The Cooper laboratory has also identified neogenin as a key regulator of adult neurogenesis by showing that it synchronises stem cell self-renewal and differentiation into new neurons.

Another project in the laboratory is aimed at developing a novel class of nanoparticles as an effective drug delivery system for the treatment of neurodegenerative disease. In collaboration with Professor Perry Bartlett (QBI), Professor Max Lu and Dr Zhi Ping Xu of the Australian Institute for Bioengineering and Nanotechnology, they have demonstrated that these nanoparticles can efficiently deliver drugs to neurons within the adult mouse brain.



Neurons are functionally integrated into the established circuitry of the olfactory bulb of the adult mouse.

Associate Professor Helen Cooper is a QLD Smart Futures Fellow.

Laboratory Head **Associate Professor Elizabeth Coulson**

Memory updating in progress. With mice having previously learned the location of the hidden escape platform (pink) within a pool of opaque water, the mouse must now learn a new platform location (yellow). The swim path of the mouse is shown in red over 3 trials and improves each time. Memory updating is impaired in a mouse model of Alzheimer's disease, with mice failing to progress from the first behaviour. Image Zoran Boskovic.

2012 Laboratory Members L-R: Elizabeth Coulson, Fabienne Alfonsi, Earlene Ashton, Zoran Boskovic, Sophie Hill, Dusan Matusica, Linda May, Nick Palstra, Aanchal Sharma, Sune Skeldal, Toni Turnbull. *Not pi*ctured: Georg Kerbler, Mirela Wagner. **Background**: Candidate treatment for neurodegeneration causes growth of axons from a cluster of neurons grown in tissue culture. The β-III tubulin neuronal filament is stained green to show the axons. Image Dusan Matusica.

Promoting neuronal survival to treat dementia and neurodegeneration

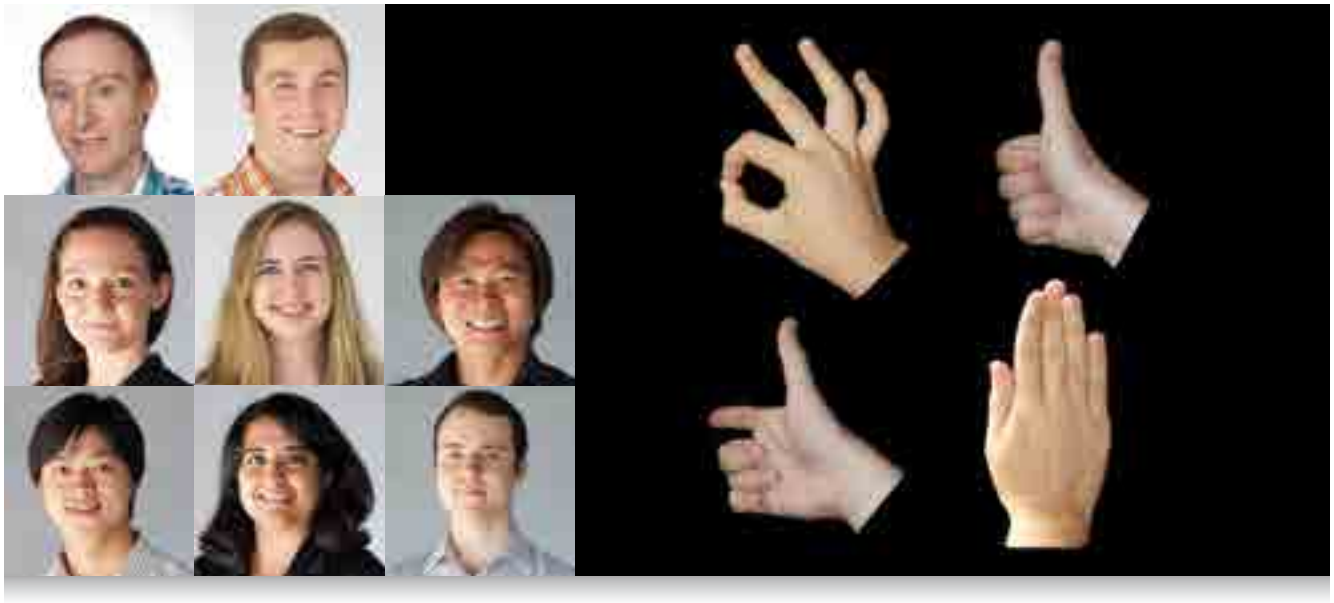
The Coulson group aims to understand the factors which promote the survival of nerve cells throughout the life of the organism. By understanding the molecular and environmental factors that control neuronal survival, the group's goal is to develop molecules that can mimic naturally occurring mechanisms to treat neurodegenerative diseases.

The main feature of Alzheimer's disease, the most common form of ageing dementia, is cognitive decline. The impaired memory and navigation that is often seen in people with Alzheimer's disease is caused by degeneration of neurons in particular areas of the brain. The Coulson laboratory has delineated a key molecular pathway by which this neuronal degeneration occurs. It has demonstrated that this pathway is normally regulated by neurotrophic factors, the production of which declines in humans as they age.

In one series of experiments, members of the Coulson laboratory have identified biochemical features that regulate the normal balance of survival and cell death signalling initiated by the p75 neurotrophin receptor. They found that two different co-receptors can influence the actions of p75 neurotrophin receptor by changing how the receptor is processed by cellular enzymes.

By studying the molecular decision making processes of the p75 neurotrophin receptor-mediated pathways, they also discovered a molecule that can enhance the survival actions of neurotrophic factors, mimicking a normal function of p75 neurotrophin receptor.

Their molecule can trick the old neurons into acting as through they are exposed to the same amount of growth factors as young neurons, thereby keeping them alive and enabling them to grow their neuronal connections. The Coulson laboratory are currently using this molecule in animal models of neurodegeneration to test whether it can prevent neuronal degeneration and thus memory impairment.



2012 Laboratory Members L-R: Ross Cunnington, Jeffery Bednark, Veronika Halász, Emily Hielscher, Kian Ng, Vinh Nguyen, Simmy Poonian, Chase Sherwell. *Not pic*tured: Marta Bortoletto, Yuan Cao, Doug Fraser, Luis Sebastian Contreras Huerta. **Background:** Examining brain processes for our ability to understand others' actions and gestures.

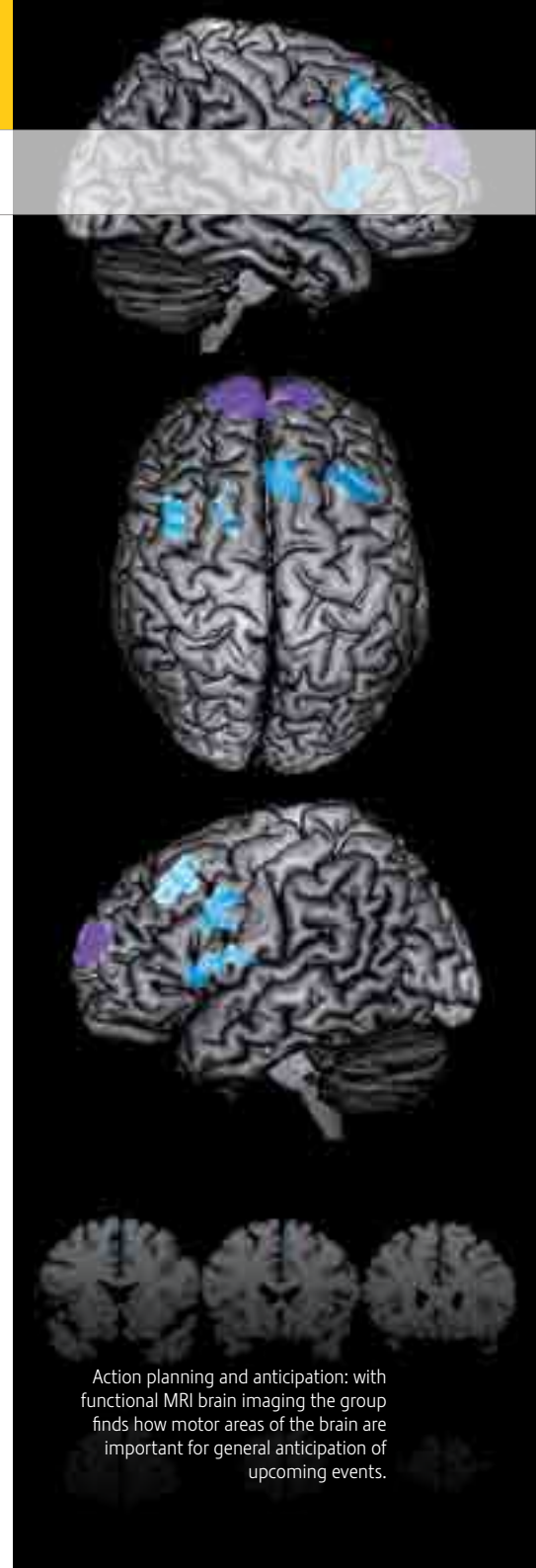
Brain processes for understanding others' actions

The Cunnington laboratory focusses on the brain processes involved in perceiving and understanding the actions of others, as well as planning and preparing for our own voluntary actions. Whenever we observe another person's actions, gestures or emotions their states appear to be "mirrored" in our own brain, leading us to understand their actions, intentions and emotions through a process of simulation or mirroring.

Research from the Cunnington laboratory has revealed how specialised regions of the brain are important for decoding the intentions or goals of people's actions. These regions appear to process and detect changes in people's actions automatically, even when our attention is focussed elsewhere, so that we are very quick to understand people's goals and to detect when their actions were unexpected.

By using brain imaging methods to study responses to faces and facial emotions, the Cunnington group is discovering how mirroring processes lead us to empathise with others and share a little of their emotion. Controversially, this neural empathy appears to be stronger when we see people of our own race express emotion than when seeing people of a different race express the same emotion. The Cunnington group is examining how this bias in neural empathy or mirroring changes with learning and familiarity with other races.

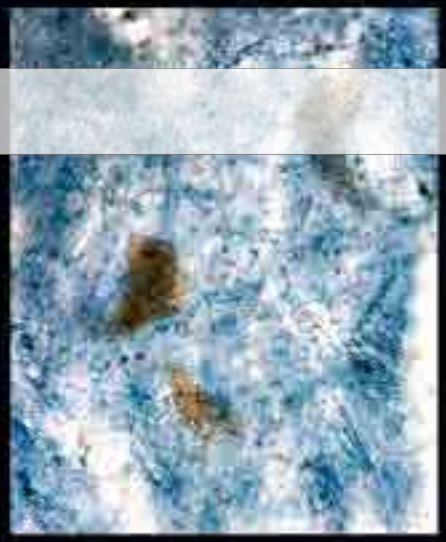
The group is also combining electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) to model the dynamics of brain function during action and perception. The group is examining the dynamic interactions between brain areas that are important for the perception of faces, actions and gestures. It is also using machine-learning computational methods to decode brain activity to predict decisions for actions, and using high-resolution imaging to examine the circuits of the brain that are crucial for the co-ordination of voluntary actions.

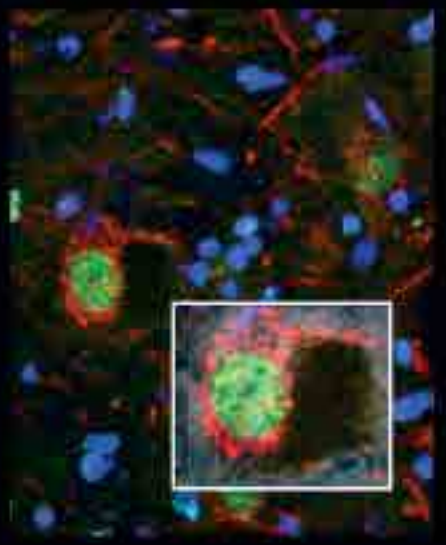


Action planning and anticipation: with functional MRI brain imaging the group finds how motor areas of the brain are important for general anticipation of upcoming events.

Associate Professor Ross Cunnington holds a joint appointment with the School of Psychology.

Laboratory Head **Associate Professor Darryl Eyles**





Above: Brightfield microscopy image of the human substantia nigra showing dark neuromelanin pigmented dopaminergic neurons.

Below: The inset is a higher magnification image of a neuron, fluorescently dual labelled for the rate-limiting enzyme responsible for dopamine synthesis, tyrosine hydroxylase (red), and the nuclear vitamin D receptor (green).

2012 Laboratory Members L-R: Darryl Eyles, Suzanne Alexander, Xiaoying Cui, Pauline Ko, David Kvaskoff, Emilia Lefevre, Pei-Yun Ashley Liu, Henry Simila. *Not pictured:* Kerry Gilespie, Peter Josh, Aung Aung Kywe Moe. **Background:** Associate Professor Darryl Eyles (left) and research technician Mr Cameron Anderson viewing a dried blood spot, which is used in assays linking DVD-deficiency with MS/schizophrenia/autism.

Vitamin D and brain development

The Eyles laboratory focusses on how known risk-factors for schizophrenia, including developmental vitamin D (DVD) deficiency, change the way the brain develops. The Eyles group has developed an extremely sensitive LC/MS/MS assay for vitamin D species in blood spot cards. This assay allowed the landmark study in 2010 implicating maternal levels of vitamin D as a risk factor for schizophrenia to be conducted. This finding has recently been replicated in a larger population. This assay is also now being used to investigate whether low vitamin D at birth also predicts later onset of autism and multiple sclerosis.

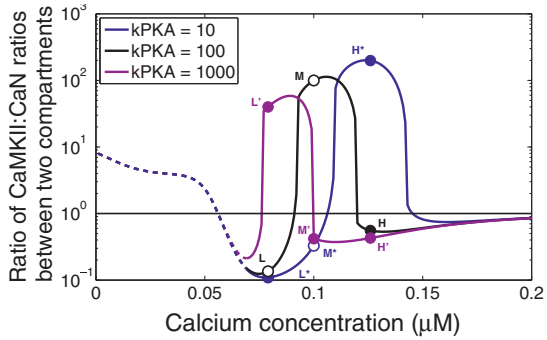
Over the past 13 years the Eyles group have been exploring the role of vitamin D in the developing brain and how DVD-deficiency may affect brain function and behaviour in adult offspring.

In 2005 the group established the distribution of the vitamin D receptor (VDR) in the human brain, and have more recently mapped the ontogeny of this receptor in the brains of experimental animals. They show the rich distribution of this receptor in dopamine neurons in both experimental animals and humans (image left).

Schizophrenia is also closely associated with abnormalities in dopamine transmission. The Eyles group's work in DVD-deficient animals confirms there are early abnormalities in dopamine development and turnover, and their work in human cell systems describes the direct control vitamin D exerts over dopamine production via the VDR.

The group has fast-tracked some of their discoveries in rodent models into other model systems, including the fruit fly and zebrafish, and has established models of restricted early transient impairments in dopaminergic development, which may be of aetiological relevance to what happens in the developing human brain in schizophrenia. Collectively, their work represents a synthesis of the two major theories of schizophrenia – "dopamine hypothesis" and "neurodevelopmental hypothesis" into the "dopamine ontogeny hypothesis of schizophrenia".

Associate Professor Darryl Eyles holds a conjoint appointment with Queensland Health.



2012 Laboratory Members L-R: Geoffrey Goodhill, Lilach Avitan, Maria Caldeira, Kelsey Chalmers, Richard Faville, Clare Giacomantonio, Nicholas Hughes, Jonathan Hunt, Elizabeth Kita, Huyen Nguyen, Zac Pujic, Biao Sun, Daniel Sutherland. *Not pictured:* Clement Bonini, Elizabeth Forbes. **Background:** The response of axons to gradients predicted by a mathematical model.

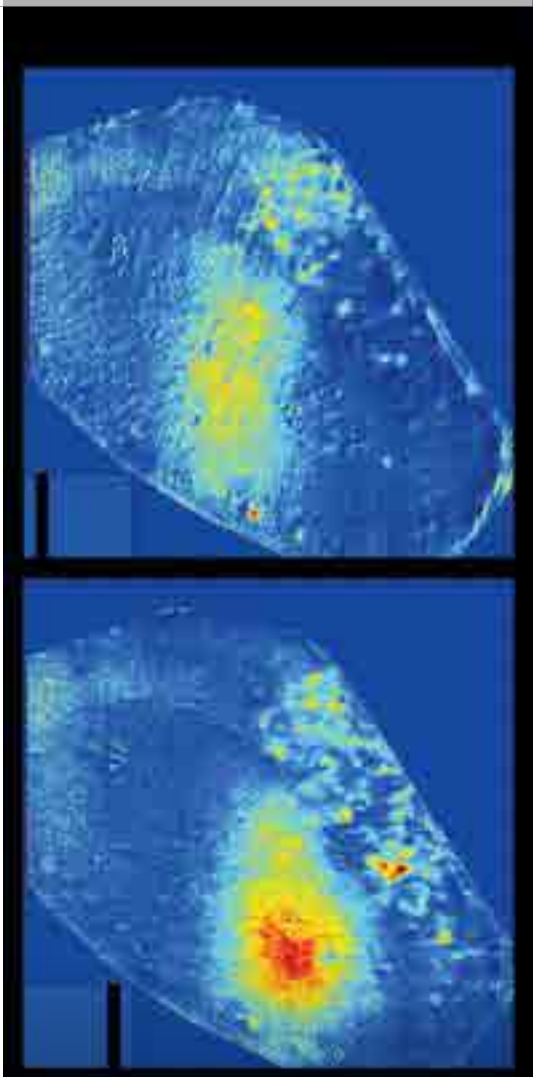
Mathematical models to understand brain wiring

For the brain to function properly, its neurons must be connected correctly. Research in the Goodhill laboratory uses a unique combination of experiments and theoretical modelling to develop a computational understanding of how the nervous system becomes wired up during development. The laboratory's guiding philosophy is that building mathematical models allows a much more precise understanding of the underlying phenomena than relying on purely qualitative reasoning.

One area of focus for the group is how nerve fibres (axons) are guided by molecular gradients to find appropriate targets in the developing nervous system. The laboratory recently developed a theoretical model to understand quantitatively how levels of calcium and cAMP in axons determine whether they are attracted or repelled by guidance cues. The model made surprising predictions that the group confirmed experimentally. This may help to explain the behaviour of developing and regenerating axons *in vivo*.

The laboratory has also investigated the shape of growth cones, the structures at the tip of developing axons. This morphology is complex and highly dynamic but the significance of these changes for either the sensory or motor roles of growth cones is mostly unknown. Sophisticated mathematical techniques for characterising shape in general are currently being adapted in order to develop a more quantitative understanding of the role growth cone shape plays in effective axon guidance.

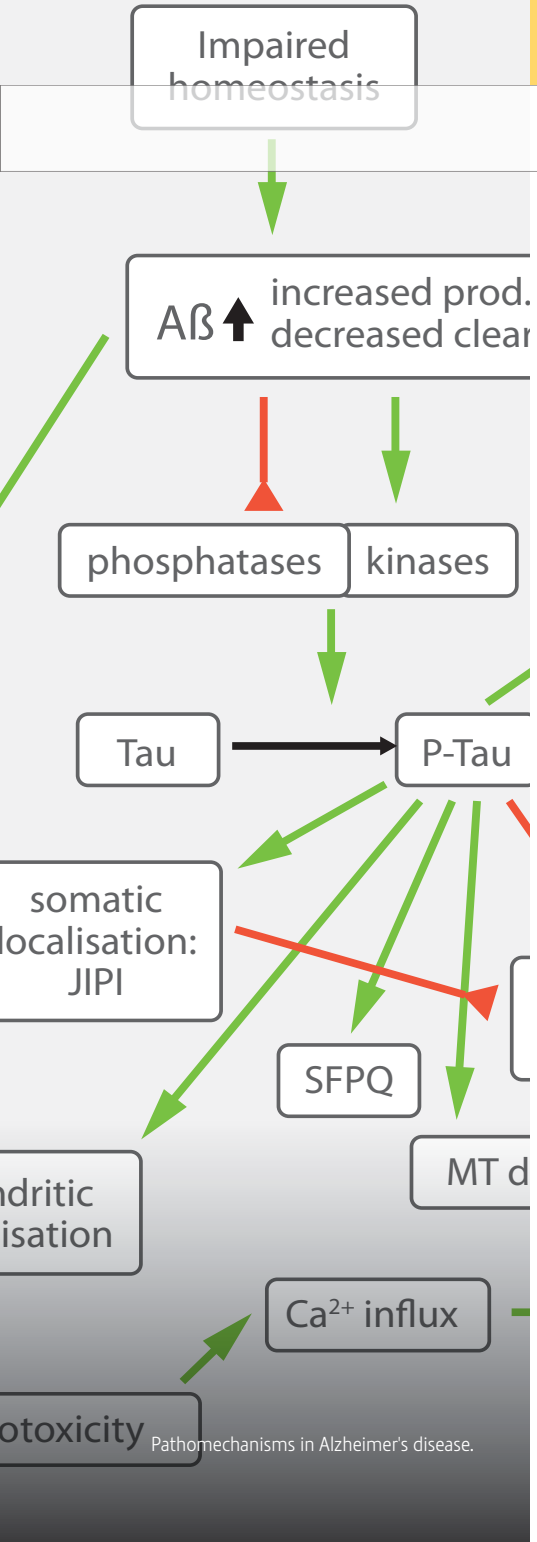
The group is also using fluorescent labelling techniques to visualise the simultaneous activity of many neurons in the developing zebrafish brain in response to simple visual stimuli. Using mathematical techniques from statistics and information theory it is then possible to predict how the zebrafish could optimally decode these patterns of activity in order to determine what visual stimulus was actually present. A better understanding of neural decoding is important for optimising the design of brain-computer interfaces.



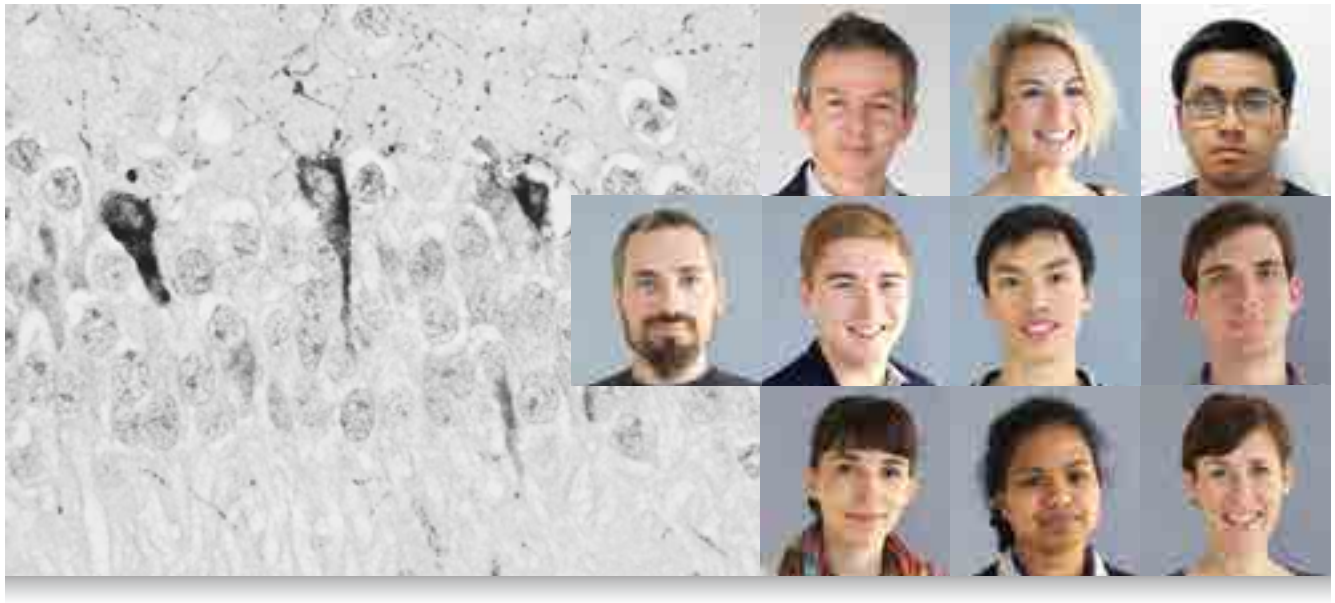
Activity in the zebrafish brain in response to visual stimuli at different positions.

Professor Geoffrey Goodhill holds a joint appointment with the School of Mathematics and Physics.

Laboratory Head **Professor Jürgen Götz**



Pathomechanisms in Alzheimer's disease.



2012 Laboratory Members L-R: Jürgen Götz, Sian Baker, Xia Di, J Bertran-Gonzalez, Harrison Evans, Hon Mun Lee, Gerhard Leinenga, Miriam Matamales, Tishila Palliyaguru, Linda Wernbacher. *Not pictured:* Julia Gutmann. **Background:** Neurofibrillary tangles in a transgenic mouse model of Alzheimer's disease.

Understanding the mechanisms of neurodegenerative disorders

At present there is no cure for Alzheimer's disease and other forms of dementia. This poses an unprecedented social and economic challenge to Australia, a country with the second highest life expectancy worldwide.

In the Götz laboratory, which forms part of the Centre for Ageing Dementia Research, there are four major streams of research: (1) understanding the pathogenic mechanisms of key players in dementia, such as the microtubule-associated protein TAU; (2) understanding the normal, physiological roles of proteins implicated in disease, such as TAU; (3) developing novel tools or methods to visualise *de novo* protein synthesis or to get drugs past the blood-brain barrier; and (4) developing biomarkers and therapies for treatment.

In a collaborative effort with Professor Mel Feany from Harvard University, in 2012 the group discovered that TAU causes an elongation of the mitochondria, the powerhouses of the cell, resulting in neuronal death. This work was published in *Neuron* and was further highlighted by *Cell*.

During the year, Professor Götz and his team also successfully established a novel click chemistry method in *C. elegans* that allows for the visualisation and identification of newly synthesised proteins. The group plans to use the new method to determine the role of TAU at the synapse and in memory functions. Again in *C. elegans*, they demonstrated that the *C. elegans* homologue of TAU, PTL-1, is important for the maintenance of neuronal morphology in ageing.

In a study published in *PLoS ONE* and selected for Faculty of 1000 Biology, the group demonstrated mislocalisation of a nuclear factor, SFPQ, in relation to TAU pathology, a finding they validated in brain tissue from patients with Alzheimer's disease. This suggests that one effect of TAU aggregation and mislocalisation in neurodegenerative disorders may be related to mislocalisation of nuclear factors.

2012 Laboratory Members L-R: Massimo Hilliard, Justin Chaplin, Sean Coakley, Rosina Giordano, Rhianna Knable, Casey Linton, Ellen Meelkop, Brent Neumann, Annika Nichols, Nicholas Valmas. *Not pictured:* Paula Mugno, Cara Nolan, Phoebe Watt. **Background:** A colour-rendered fluorescence image of a *Caenorhabditis elegans* carrying a dominant mutation in the gene encoding for MEC-7/β-Tubulin.

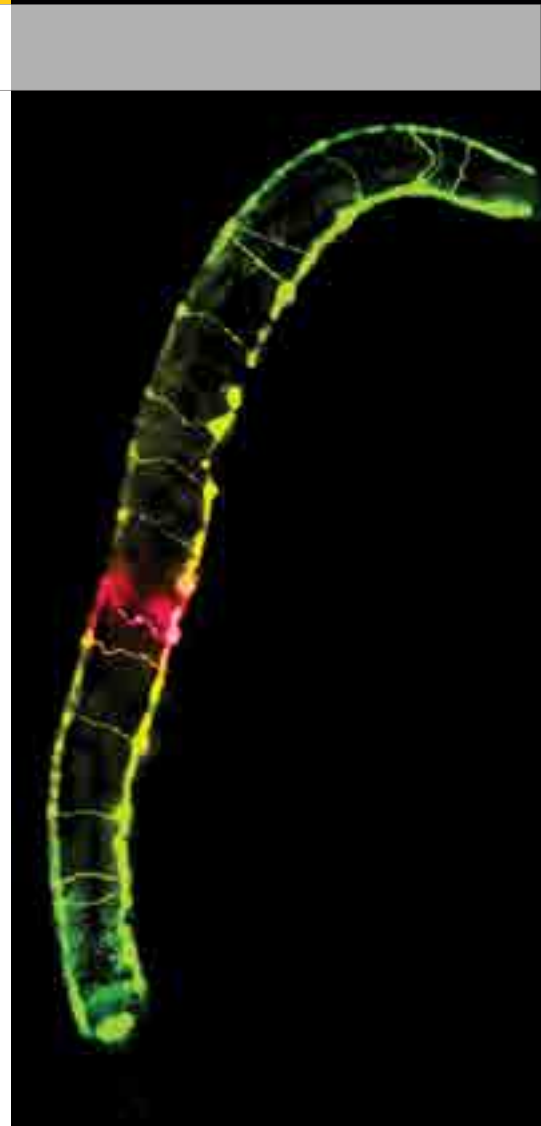
Axonal development, maintenance and regeneration: molecules & mechanism

Determining how individual neurons develop is crucial for understanding how highly complex neuronal structures, such as the brain and spinal cord, are formed. The Hilliard laboratory is interested in understanding how axons (nerve fibres conducting impulses from the neuron) and dendrites (nerve processes conducting impulses to the neuron) develop and how they are guided to their targets. The group also investigates how axonal structure is maintained over time and how it can be reconstituted after injury.

Neurons are highly polarised cells with neurites, dendrites and axons, forming distinct morphological and functional domains. How a neuron decides exactly how many neurites to extend is not well understood. Using *C. elegans* mechanosensory neurons as a model system, the Hilliard group has discovered MEC-7/β-Tubulin, a component of the microtubules, to have a critical role in this process. In contrast to the idea that microtubules are simple building blocks or cargo-tracks of the cytoskeleton, these results *in vivo* are consistent with emerging evidence *in vitro* that microtubules can provide critical signals for axon formation.

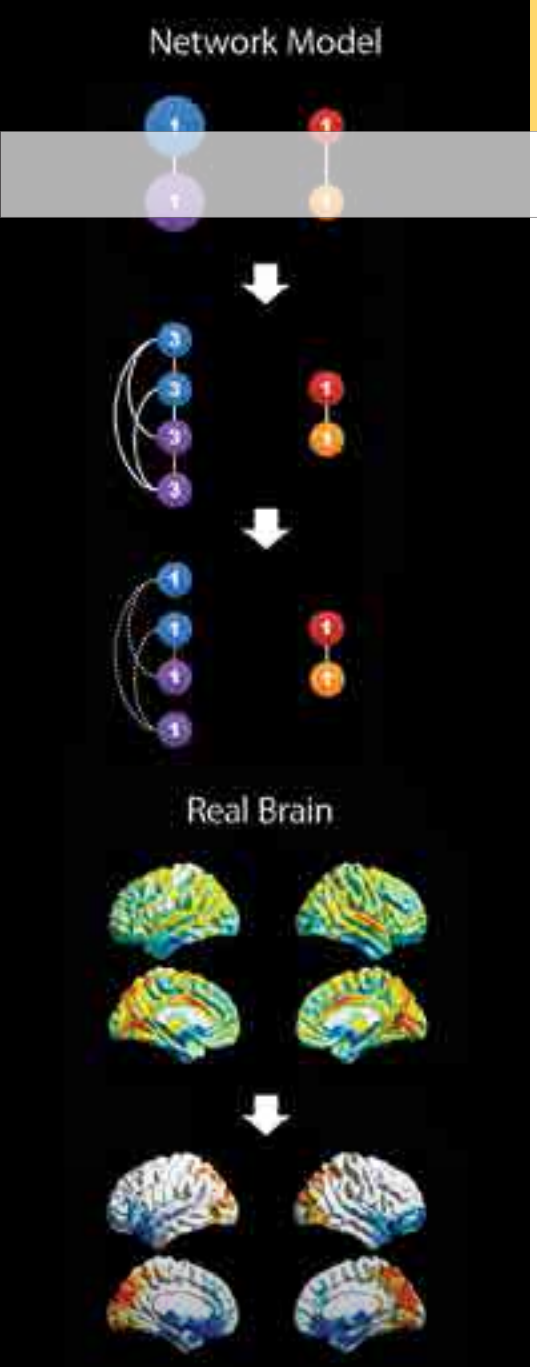
The axon is the neuron's longest process, but the mechanisms that allow it to maintain its structural integrity and its regeneration capacity following injury are still poorly understood. The Hilliard group have identified mutant animals in which the axons of *C. elegans* mechanosensory neurons spontaneously degenerate. Molecular identification of one of these genes has revealed a high level of conservation across animal phyla, including humans.

Using a laser-based technology to axotomise single neurons in living *C. elegans* animals, the team has also characterised neuronal regeneration in different classes of sensory neurons. They have shown that axonal regeneration can occur by a mechanism of axonal fusion, whereby the two separated axonal fragments can specifically re-attach and restore the original axonal tract.

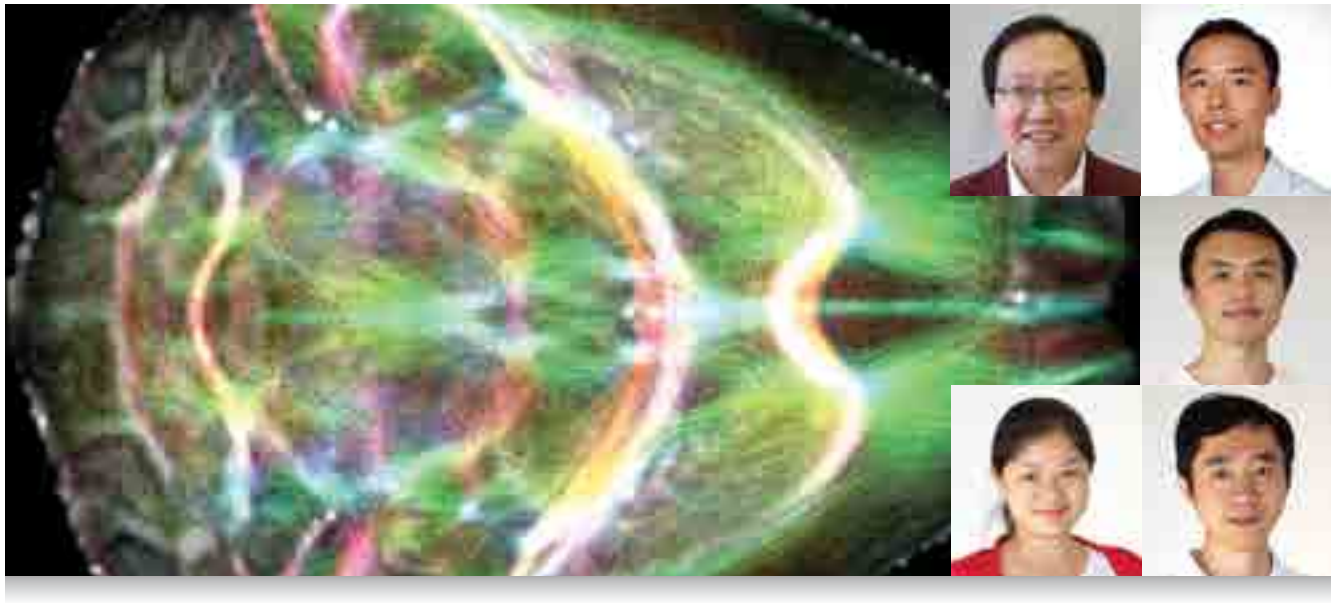


A colour-rendered fluorescence image of *C. elegans* GABAergic motor neurons forming a ladder-like shape in the animal's body (head of the animal is on the lower left). In this mutant animal the axon, highlighted in red, is shorter, is detached from the dorsal cord, and is degenerating. Image Nick Valmas.

Laboratory Head **Professor Tianzi Jiang**



The brain hubs are affected by functional region sizes in the voxel-wise functional brain network. The group proposed an effective strategy to restore the brain architecture.



2012 Laboratory Members L-R: Tianzi Jiang, Yonghui Li, Cirong Liu, Tong Wu, Xianfeng Yang. **Background:** A diffusion MRI (dMRI) image of a mouse brain.

Mapping human and animal brain networks with neuroimaging

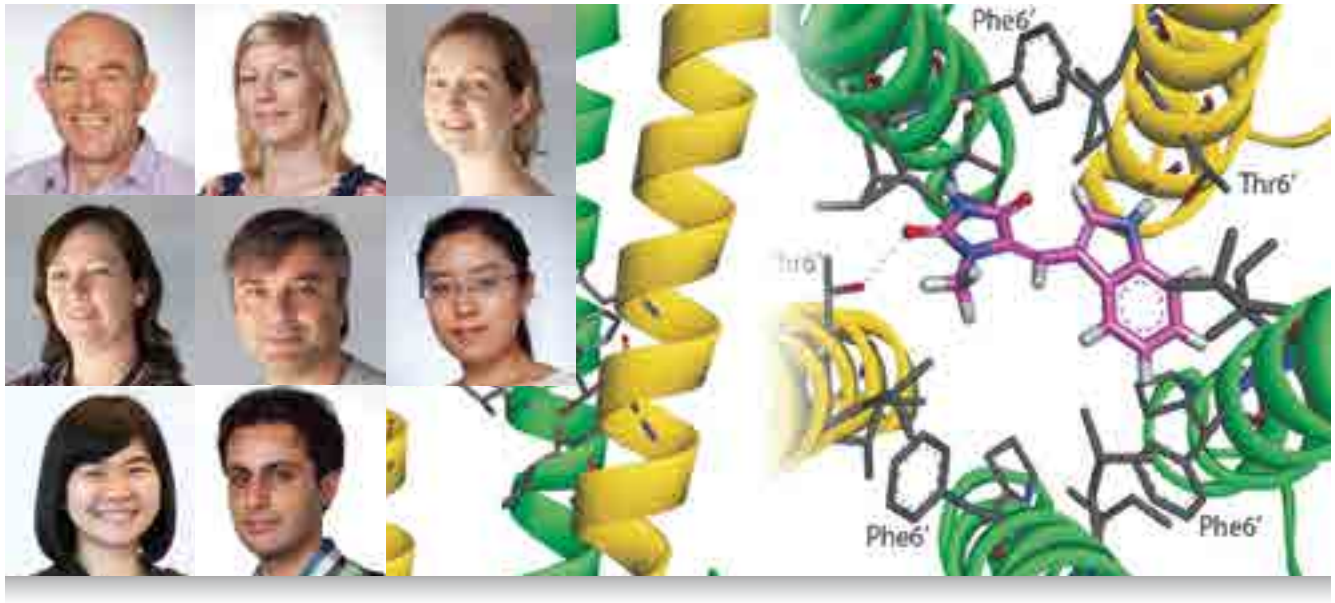
Convergent evidence has shown that brain functions can manifest on brain networks on different scales, and that the brain malfunctions associated with most psychiatric disorders are the result of faulty brain networks. The "Brainnetome" (www.brainnetome.org) is an emerging avenue to integrate the multi-level network features obtained with various functional and anatomical brain imaging technologies on different scales.

The Jiang laboratory is studying basic theory, methodologies and algorithms underpinning the brainnetome platform, and their applications in neurological and psychiatric diseases. In 2012, their research followed two streams.

The first involved the human brainnetome. The stream aimed to solve a key problem in the voxelwise functional brain network. The team quantitatively evaluated how the size of functional regions distorts the degree of centrality in the voxelwise brain network and proposed an effective strategy to correct this distortion, which can restore the true brain network architecture. In another study the group developed an automated subcortical segmentation pipeline and a brain shape analysis method by diffeomorphic metric mapping using stationary velocity. The proposed method can be used to analyse shape variability of populations with brain diseases and different genotypes, for example.

The second research stream involved the mouse brainnetome, focussing on the Disrupted-In-Schizophrenia-1 (*DISC1*) gene. Using four different strains of *DISC1* mice, the Jiang laboratory have shown that white matter fibres across the whole brain can be reconstructed using a probabilistic tractography method based on diffusion MRI data acquired from a high field small animal magnetic resonance imaging system. In particular, fine fibre architecture between the cortex and subcortical regions can be easily identified, which means the group can now map and characterise the structural connectivity/network of the mouse brain at high resolution.

Professor Tianzi Jiang holds a joint appointment with the Centre for Advanced Imaging.



2012 Laboratory Members L-R: Joe Lynch, Anna Bode, Christine Dixon, Justine Haddrill, Angelo Keramidas, Han Lu, Ming Shiuan Soh, Sahil Talwar. *Not pictured:* Suzanne Scott, Azra Zamri, Yan Zhang, Qian Wang. **Background:** A molecular model of a glycine receptor pore showing a new drug (pink) isolated from a marine sponge binding potently to its site.

Targeting inhibitory neurotransmitter receptors in neurological disorders

The Lynch laboratory's major research interest concerns the molecular structure and function of the glycine and $GABA_A$ receptor chloride channels that mediate inhibitory neurotransmission in the brain. The $GABA_A$ receptor is an important therapeutic target for sedative and anxiolytic drugs and the glycine receptor has recently emerged as a therapeutic target for pain, spasticity, epilepsy and tinnitus. The Lynch group is attempting to identify the locations of drug binding sites on these receptors. They are also discovering new drugs active at these receptors, which could lead not only to improved therapies but also to better tools for basic research.

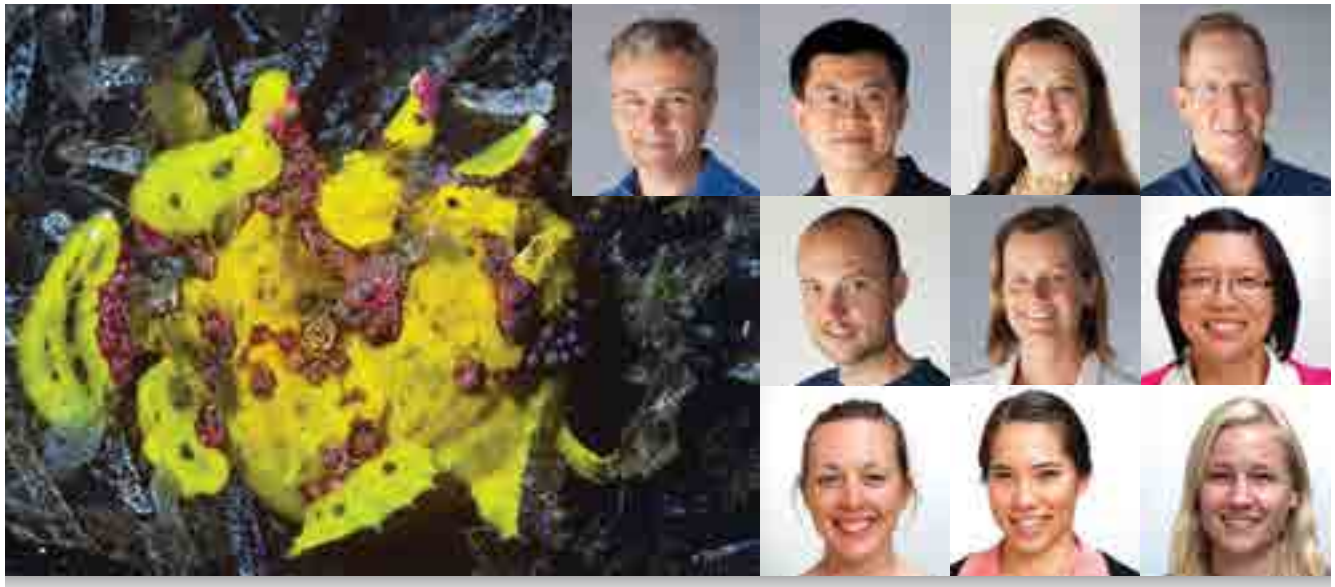
For several years the laboratory has been attempting to develop novel analgesics for chronic inflammatory pain that work by targeting spinal cord glycine receptors. In collaboration with Professor Rob Capon's group at the Institute for Molecular Bioscience, they have recently discovered a new drug that binds to glycine receptors with an extremely high affinity and produces potent analgesia in rats. This will serve as an excellent lead compound to develop new therapies for chronic pain.

Hyperekplexia (or startle disease) is a rare human neurological disorder that produces an exaggerated startle in response to unexpected auditory or tactile stimuli. In collaboration with geneticists at the University of Swansea, the laboratory has recently shown that the glycine receptor beta subunit is an important new protein targeted by hereditary startle disease mutations.

Atomic force microscopy images of antibodies attached to glycine receptors.

Laboratory Head **Professor Justin Marshall**

Above: The eyes of a mantis shrimp and the internal neural structure of the brain, optic lobes and eyes as revealed through fluorescent labelling. Below: The mantis shrimp.



2012 Laboratory Members L-R: Justin Marshall, Wen-Sung Chung, Angela Dean, Alan Goldizen, Martin How, Diana Kleine, Yi-Hsin Lee, Genevieve Phillips, Rachel Templin, Hanne Thoen. *Not pictured:* Fabio Cortesi, Fanny deBusserolles, Adrian Flynn, Simon Gingins, Amy Newman, Qamar Schuyler. **Background:** The frogfish uses colour for camouflage and confusion. This project interprets the way visual systems are fooled by camouflage.

Components of a visual system: through the eyes of marine organisms

The comparative study of brains and sensory systems in the outside world is the central drive for the Marshall *Visual Ecology* laboratory. The laboratory's model systems examine vision in marine animals such as mantis shrimp, squid, fish and turtles. Revealing how these animals use colour and polarisation for survival in the real world has led to discoveries that guide core principles in neuroscience and spill over into machine vision applications.

In 2012 the laboratory discovered a new form of colour vision in the animal kingdom, described a unique range-finding system in cephalopod eyes, gathered behavioural data on the giant squid *Archeteuthis dux* for the first time in its natural habitat, determined colour communication mechanisms to reveal how the coral trout got its spots, used real-time underwater polarisation cameras on the Great Barrier Reef and recorded from neurons in visual pathways new to science.

The Marshall laboratory's approach is to study all the components of a visual system; the retinal anatomy and optics of the eye, the neural connections and physiological function of receptors and interneurons and then piece these components together to guide the design of behavioural experiments that interrogate the performance and ecological relevance of animal vision.

Through working on the Great Barrier Reef the looming environmental issues of this habitat sparked the environmental education program CoralWatch. This initiative is in its 10th year and now communicates science to 25,000 people in over 80 countries. 2012 saw the publication of the second edition of *Coral Reefs and Climate Change; the guide for education and awareness.*

2012 Laboratory Members L-R: Jason Mattingley, Oliver Baumann, Luca Cocchi, Eve Dupierrix, Hannah Filmer, Oscar Jacoby, Marc Kamke, Inga Laube, David Lloyd, Natasha Matthews, Pascal Molenberghs, Claire Naughtin, David Painter, Amanda Robinson, Martin Sale, Susan Travis, Lisa Wittenhagen. *Not pictured:* Daina Dickins, Michael Dwyer, Will Harrison.
Background: Functional magnetic resonance imaging (fMRI) scans reveal distinct patterns of brain activity during a complex reasoning task.

Understanding how the brain sees, thinks and acts

In 2012, researchers from the Mattingley group made several important discoveries.

Mr Will Harrison showed that the brain anticipates each eye movement ("saccade") a fraction of a second before it occurs. He discovered that a perceptual phenomenon known as "visual crowding" is reduced for objects in peripheral vision that are the target of an impending saccade. He also showed that pre-saccadic updating of visual scenes preserves the elementary features of objects at their predicted post-saccadic locations. These discoveries shed new light on how the human visual system maintains a stable representation of the world, and explain why certain brain disorders cause problems with visual perception.

Dr Luca Cocchi investigated how neural networks coordinate their activity during complex, cognitive reasoning tasks. Participants were given a verbal rule and asked to indicate whether simple statements could break the rule. Using functional magnetic resonance imaging, Dr Cocchi showed that as the number of variables to be considered increased so too did the patterns of information exchange between distinct brain networks. His findings suggest that errors in human reasoning relate to fundamental limits in the brain's processing of information. They also provide clues as to why patients with neurological disorders can experience difficulties performing simple reasoning tasks.

Neural plasticity is crucial for learning and memory. Drs Marc Kamke and Martin Sale used transcranial magnetic stimulation to induce plasticity in an area of the brain responsible for controlling muscles in the hand. While undergoing the procedure, participants engaged in visual attention tasks or watched short movies of hand actions being performed by an actor. The researchers found that the amount of plasticity in the motor cortex was strongly influenced by these cognitive processes. This discovery may assist therapists to maximise the benefits of physical rehabilitation with stroke patients.

Participant prepared for electro-encephalography, with electrodes attached to the scalp to measure brain activity during a series of cognitive tests.

Professor Jason Mattingley holds a joint appointment with the School of Psychology.

Laboratory Head **Professor John McGrath**

2012 Laboratory Members, top-bottom: John McGrath, Henry Simila. *Not pictured:* Peter Josh. **Background:** Henry Simila working in the McGrath laboratory.

Early life vitamin D influences brain development.

Modifiable risk factors for schizophrenia

The aim of the McGrath group is to explore risk factors that are linked to schizophrenia. In particular, they focus on nongenetic factors that are potentially modifiable. In recent years the QBI-based team has been examining the impact of low vitamin D (the 'sunshine hormone') during early brain development and on adult brain function. In collaboration with Associate Professor Darryl Eyles and Dr Tom Burne, they have developed animal models that examine the impact of low vitamin D during gestation on brain development. In collaboration with researchers in Denmark, the United Kingdom and the Netherlands, the group is exploring the association between vitamin D levels and later mental illness.

To date, the group has clearly shown that low vitamin D during early life alters brain development in rodents, however, they will now explore whether this is also relevant to humans by investigating the association between vitamin D concentrations at birth and later risk of schizophrenia. Like folate and spina bifida, if vitamin D is linked to the risk of schizophrenia, then it offers the opportunity to use safe and readily available supplements to reduce the incidence of this disorder. The research team at QBI has pioneered this innovative hypothesis and are the world-leaders in this field.

In 2011, using animal models, they demonstrated that advanced paternal age was associated with mutations in genes linked to autism and schizophrenia. In collaboration with researchers in Sweden, the group have now shown that the offspring of older fathers, and older grandfathers, have an increased risk of autism and schizophrenia. Age of parenthood is increasing in many societies and it is feasible that paternal-age related genetic mutations will increase in the years ahead.

Professor John McGrath holds a conjoint appointment with Queensland Health.

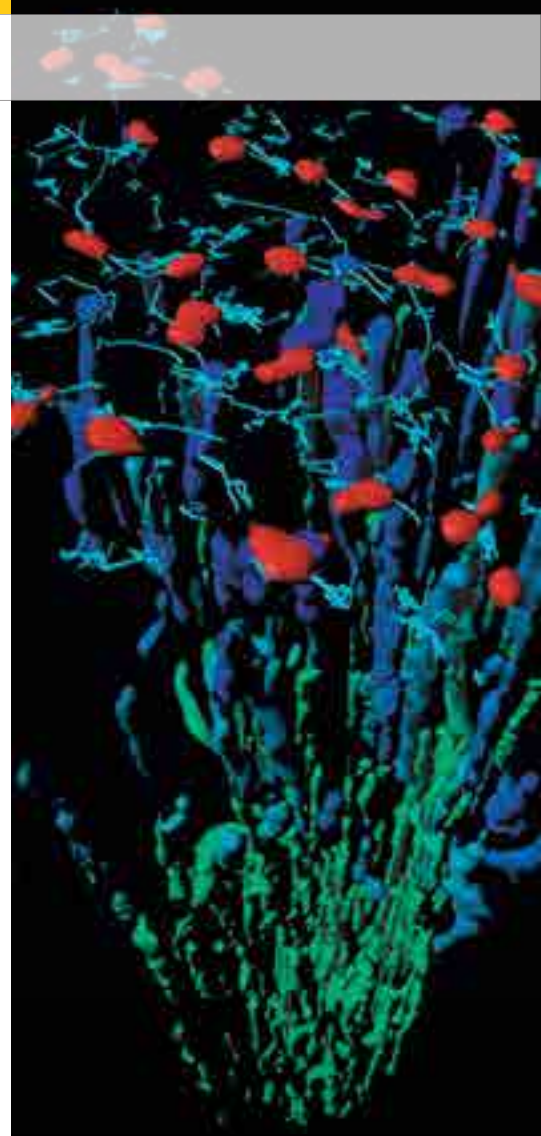
2012 Laboratory Members L-R: Frederic Meunier, Rachel Gormal, Callista Harper, David Kvaskoff, Regine C Low, Nancy Malintan, Sally Martin, Nika Mohannak, Vinod Narayana, Tam Nguyen, Shona Osborne, Andreas Papodopulos, Vanesa Tomatis, Tong (Iris) Wang. *Not pictured:* Shi (Priscilla) Goh, Ravikran Kasula. **Background:** Super-resolved image of VAMP2 labelling in cultured neurons. VAMP2 is a protein located on synaptic vesicles that is necessary for their fusion with the plasma membrane to release neurotransmitter. Image Callista Harper.

Deciphering the mechanism underpinning neuronal communication

In 2012, the Meunier laboratory focussed on the major role played by vesicular trafficking in health and disease.

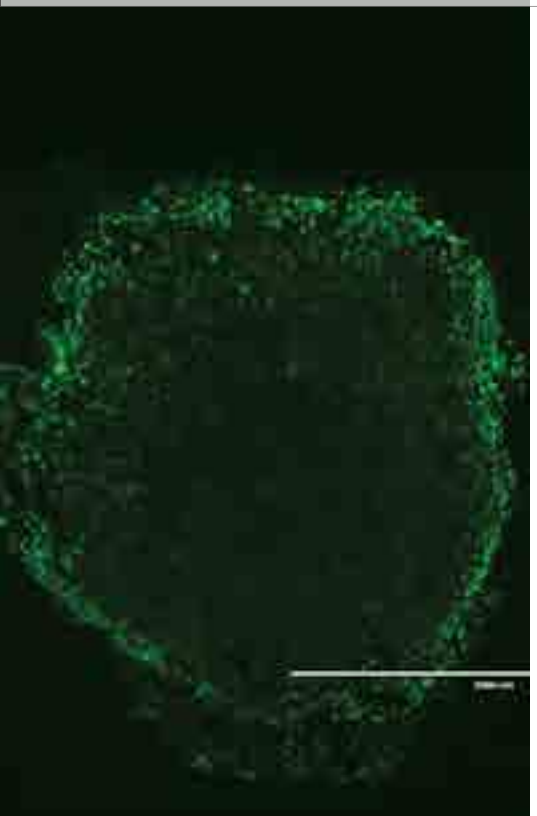
The group demonstrated that myosin VI is key to capturing secretory vesicles containing neurotransmitter and hormones on their way to the plasma membrane where they undergo fusion. These results show that myosin VI orchestrates the recruitment of secretory vesicles on the cortical actin network abutting the cell surface. These findings explain how stimulation not only triggers the release of neurotransmitter but also drives a number of intracellular processes culminating in the recruitment of new vesicles to the plasma membrane, thereby preparing for the next round of fusion. Myosin VI has been shown to be important for synaptic plasticity by regulating the formation of neurons synapses and dendritic spines. By unravelling the precise molecular mechanisms underlying the functions of myosin VI in neuroexocytosis, the team hope to be in a better position for the understanding of disorders associated with impaired function of myosin VI.

In another study, the Meunier laboratory has demonstrated that actin and dynamin cooperate to drive bulk endocytosis at the neuromuscular junction. This process allows the nerve endings to replenish their pools of synaptic vesicles containing the neurotransmitter. This novel display of presynaptic plasticity unravels how motor nerve terminals couple exocytosis with endocytosis. In collaboration with the groups of Professor Phillip Robinson (University of Sydney) and Professor Adam McCluskey (University of Newcastle), who provided the team with a highly effective dynamin inhibitor, the Meunier group has demonstrated that such drugs could be used to prevent activity-dependent bulk endocytosis.



3D-reconstruction of secretory granules (red) and their tracks (light blue) from a neurosecretory cell expressing myosin VI. The cell was imaged using total internal reflection microscopy (TIRFM) and the reconstruction was done using IMARIS software. Image Vanesa Tomatis and Andreas Papadopulos.

Laboratory Head **Professor Bryan Mowry**



Induced pluripotent stem cell colony (stained with fluorescent antibody) from a schizophrenia patient.

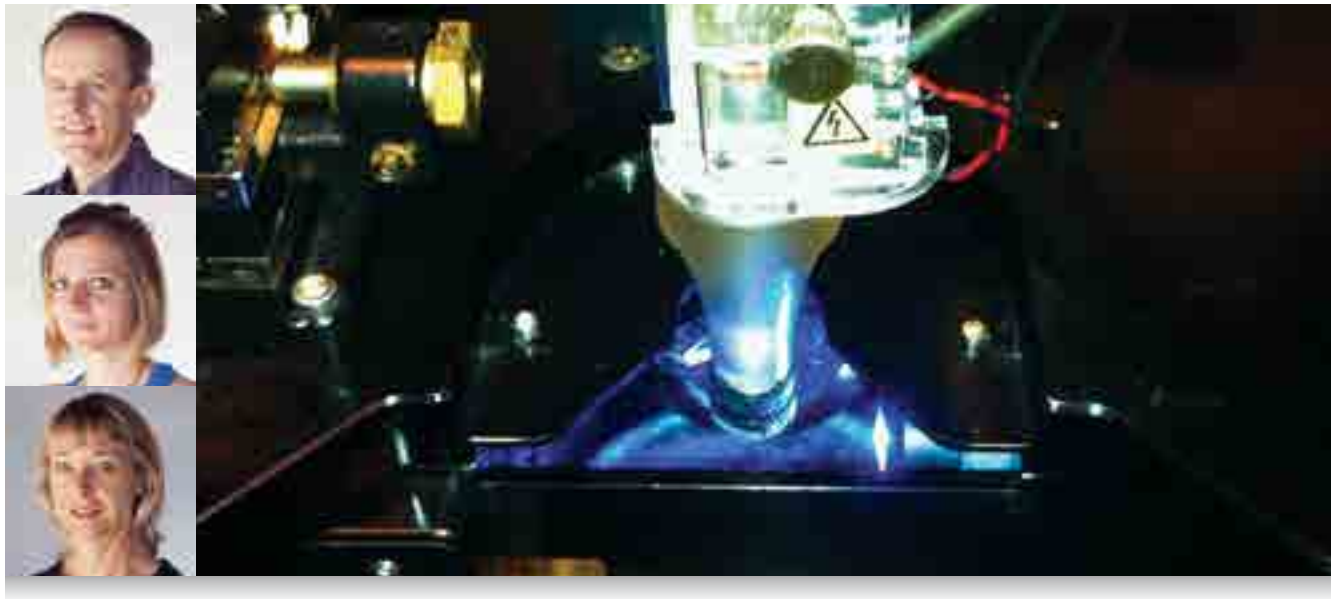
2012 Laboratory Members L-R: Bryan Mowry, Cheryl Flippich, Jake Gratten, Vasilis Mantzioris, Andrew Martin, Kalpana Patel, Chikako Ragan, Heather Smith, Xia Yao. *Not pictured:* Deborah Nertney, Yi Wang. **Background:** White matter images using diffusion tensor imaging in a patient with schizophrenia.

Genomics of psychiatric disorders

The Mowry group aims to identify and functionally characterise susceptibility genes for schizophrenia and related disorders. The group hopes to achieve this by combining genome-wide association studies (GWAS), DNA sequencing and transcriptome profiling with neuropsychological testing and neuroimaging in people with schizophrenia. Ongoing studies include (i) the recruitment of a large Indian case-control and family cohort in collaboration with Dr Thara, Schizophrenia Research Foundation, Chennai; (ii) neuroimaging and neuropsychological phenotyping of schizophrenia patients with major copy number variations, and comparing patients with a matched sample of healthy individuals; (iii) GWAS in homogeneous Indian and Sarawak populations, and relating the results to the latest European studies; (iv) transcriptome-wide analysis of small non-coding RNAs in post-mortem brain samples from schizophrenia patients and unaffected individuals; (v) targeted resequencing of a previously identified schizophrenia linkage region on chromosome 1 in an Indian case-control sample, using QBI's next-generation sequencing facility; (vi) establishment of induced pluripotent stem cells (iPSCs) in a subset of schizophrenia patients and controls to derive neuronal cells for an *in vitro* model of disease; and (vii) involvement in sample processing and analyses of the Australian Schizophrenia Research Bank data.

Highlights for 2012 include contributions to the latest Psychiatric Genetics Consortium schizophrenia GWAS that has identified in excess of 80 genetic susceptibility loci (due to be published in 2013), and publication of a perspective in *Nature Genetics* on the interpretation of *de novo* protein-coding mutations in neuropsychiatric disorders. The group published a review in *Molecular Psychiatry* on the current state-of-play in schizophrenia genetics, and is developing a neuroimmunology of schizophrenia project.

Professor Bryan Mowry holds a conjoint appointment with Queensland Health.



2012 Laboratory Members, top-bottom: Geoffrey Osborne, Anne-Sophie Bedin, Virginia Nink. **Background:** Hardware modifications to cell sorting flow cytometers allow detection of micro particles shed from cells.

Implementing novel approaches to solve fundamental problems

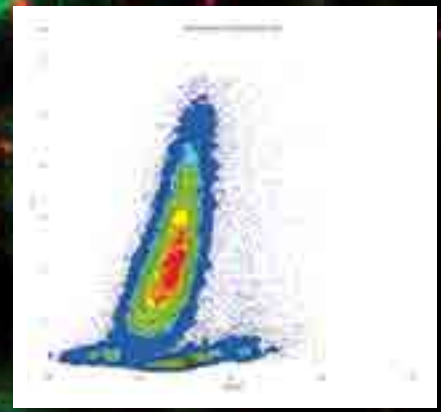
As Director of Flow Cytometry for both QBI and the Australian Institute for Bioengineering and Nanotechnology, Mr Geoffrey Osborne leads a team that provides crucial cell sorting and analysis services to researchers both within QBI and across the broader university. The laboratory specialises in the analysis and separation of cells derived from a variety of sources such as solid tissue, blood and cultured cell lines.

In 2012, investigations continued in the area of characterisation of cells from brain tumours. Investigators with an interest in brain tumours often suffer shortages of research material, as solid tissue samples are needed by clinicians for a full and proper diagnosis to be made. To address this problem, working with collaborators from the Queensland Institute of Medical Research and the Royal Brisbane and Women's Hospital, the Osborne group has shown that surgical wash bottles, used for collection of cancerous material during surgery, are rich sources of cells for research purposes.

This year also saw the laboratory involved in a publication that characterised the similarities present in stem cells from renal, cardiac and bone marrow origins. Understanding the cell surface markers present on stem cells from different lineages has provided insights that are useful in the identification and enrichment of neural stem cells.

The Osborne group was also involved in the development and characterisation of a mitochondrial reporter line, KMEL2, in human embryonic stem cells (hESCs). KMEL2 hESCs facilitate the study of mitochondria in a range of cell types and permit real-time analysis. These cells represent an ideal model system for studying neurodegenerative diseases where mitochondrial functions are affected.

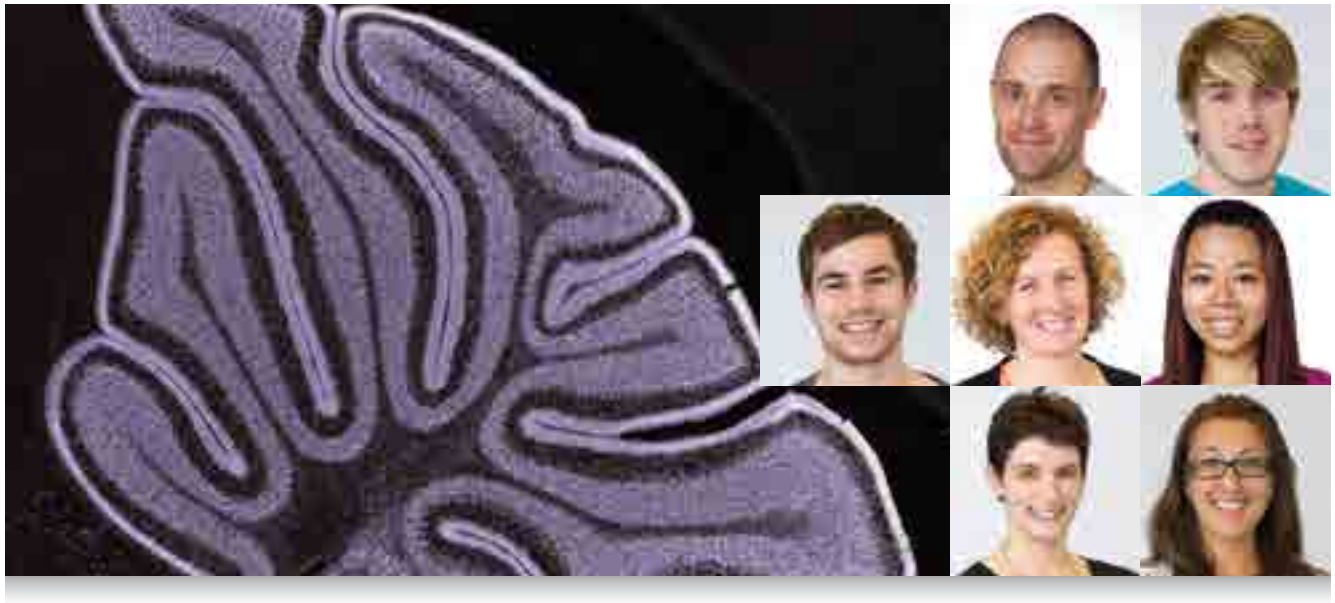
Studies into the particle entrainment and processing by flow cytometric cell sorters also continued and led to the development of novel algorithms that implement the selection of cells for separation by the instrument. This approach is now being developed for commercialisation.



Cellular subpopulations purified by cell sorting (inset) enriched for neural stem cells that divide and give rise to progeny, here immune-stained with a neuronal marker βIII-tubulin (red) and glial marker GFAP (green) and counterstained with DAPI (blue).

Mr Geoffrey Osborne holds a joint appointment with the Australian Institute for Bioengineering and Nanotechnology.

Laboratory Head **Dr Michael Piper**



2012 Laboratory Members L-R: Michael Piper, Joshua Eeles, Lachlan Harris, Tracey Harvey, Evelyn Heng, Chantelle Reid, Diana Vidovic. **Background:** Expression of the transcription factor Pax6 within the postnatal cerebellum reveals the highly convoluted architecture of this brain region. The cerebellum is involved in balance and postural control.

Cell self-renewal and differentiation

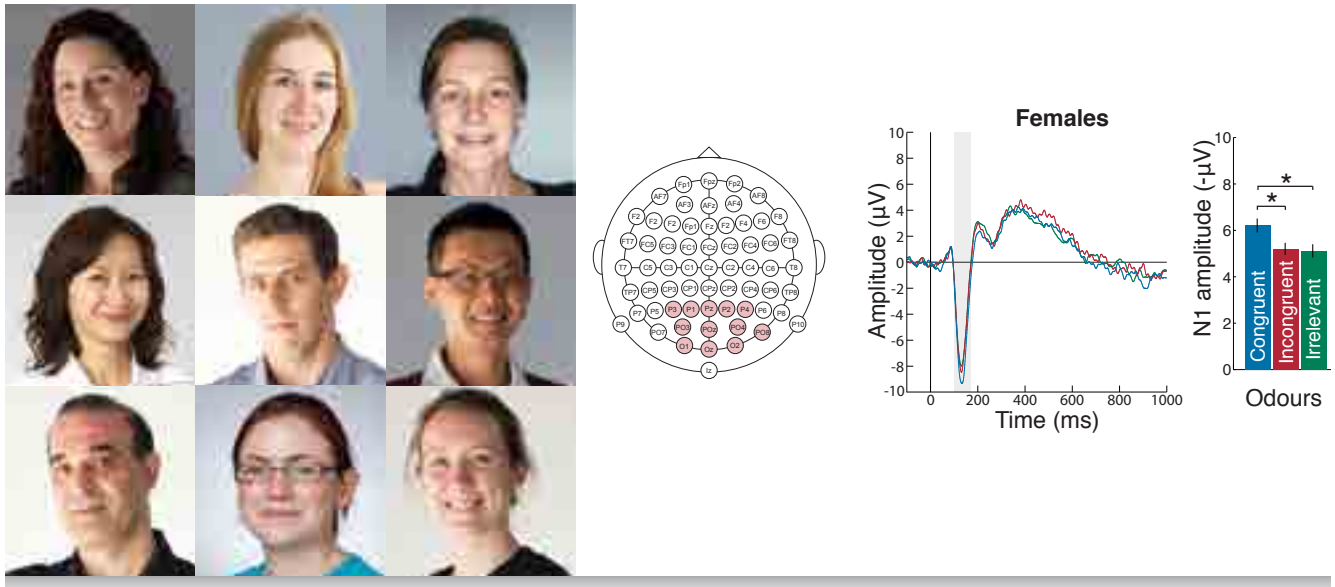
The brain is ultimately derived from neural stem cells, which differentiate to give rise to both neurons and glia within the developing and adult brain. Controlling how these neural stem cells either self-renew or differentiate is critical during development, and changes to the normal trajectory of these processes can lead to severe functional consequences. Moreover, many of the genes that control neural stem cell differentiation are misexpressed aberrantly within brain cancers such as glioma. The Piper laboratory is investigating the molecular mechanisms underlying progenitor cell self-renewal and differentiation in order to deepen our understanding of brain development and function, as well as to reveal the underlying deficits in brain cancers such as glioma. To do this it uses mouse model systems and *in vitro* cell culture paradigms to investigate the key processes behind the biology of neural progenitor cells, and to reveal the genetic hierarchy that controls neural progenitor cell differentiation.

In a paper recently published in *The Journal of Comparative Neurology*, the Piper laboratory revealed that a group of transcription factors named the nuclear factor one (NFI) family play a central role in regulating how neural progenitor cells differentiate within the developing brain. Furthermore, a study published in *The Journal of Neuroscience* gave an insight into how the NFI family does this, by revealing that NFI transcription factors repress the expression of genes central to stem cell self-renewal.

Current work in the Piper laboratory is aimed at discovering the role of NFI transcription factors in the adult brain, and their contribution to the formation of glioma.

Dentate granule cells in the hippocampus (red) play a central role in the function of this brain structure. The hippocampus is central to the processes of learning and memory.

Dr Michael Piper holds a joint appointment with the School of Biomedical Sciences.



2012 Laboratory Members L-R: Judith Reinhard, Stephanie Biergans, Julia Canning-Ure, Ming-Yu Chen, Alexandre Cristino, Shao-chang Huang, Homayoun Kheyri, Aoife Larkin, Amanda Robinson. **Background:** Schematic arrangement of electrodes measuring brain activity during inhalation of odours matching or not matching images, and results showing that in females matching odours enhance activity of early visual processing.

Uncovering mechanisms of multisensory interactions

Researchers in the Reinhard laboratory investigate how the brain processes sensory information and translates it into behavioural activity, thus linking brain function to behaviour. A particular focus is the sense of smell and its effect on behaviour and cognitive performance. The laboratory uses insect model systems in combination with human research, and integrates behavioural studies with physiological and molecular approaches.

Sensory information from our environment is initially registered within anatomically and functionally segregated brain networks, but is also integrated across modalities in higher cortical areas. Little is known about where, when and how multisensory integration in the brain works and about the effects it has on sensory perception. Recent research in the laboratory is aimed at understanding the interactions between olfaction and vision, in particular how the odours that surround us affect how we detect and perceive objects. The group recently used novel visual paradigms to show that visual attention towards an object is significantly enhanced when smelling a matching odour at the same time. The objects are detected faster and more robustly. In collaboration with Professor Jason Mattingley the team then used electroencephalography to measure brain activity in response to photographs of familiar objects when matching or non-matching odours were presented simultaneously. They discovered that matching odours significantly enhanced brain activity in visual areas only milliseconds after presentation. This suggests that olfaction has a profound influence on visual perception and this multisensory integration happens very early during sensory processing. This research indicates that olfactory and visual brain processes are more closely coupled than previously thought.

Dr Reinhard and her team are now investigating the neural correlates of olfactory-visual integration in the brain using functional magnetic resonance imaging, where people's brains are scanned while smelling odours that are presented at the same time as either matching or non-matching images.

Participant prepared for electroencephalography with electrodes attached to the scalp to measure brain activity during inhalation of odours and presentation of visual images.

Laboratory Head **Professor Linda Richards**

2012 Laboratory Members L-R: Linda Richards, Gonzalo Almarza, John Baisden, Jens Bunt, Ilse Buttiens, Maria Caldeira, Amelia Douglass, Tess Evans, Laura Fenlon, Ilan Gobius, Jonathan Lim, Samantha Liu, Yolanda Liu, Laura Morcom, Rodrigo Suarez, Dennis Yeow. *Not pictured:* Tim Edwards, Lu Zhao. **Background:** Neurons from the mouse hippocampus showing dendrites and axons in red and cell nuclei and synaptic contacts in green.

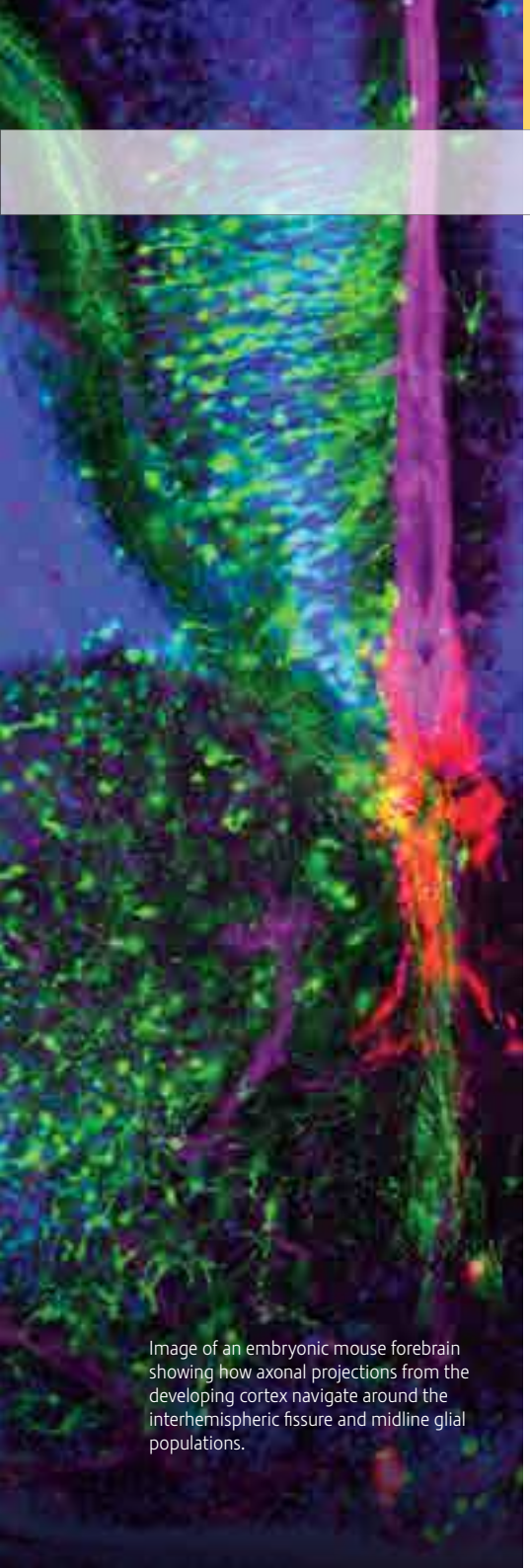


Image of an embryonic mouse forebrain showing how axonal projections from the developing cortex navigate around the interhemispheric fissure and midline glial populations.

Functional circuits in the brain

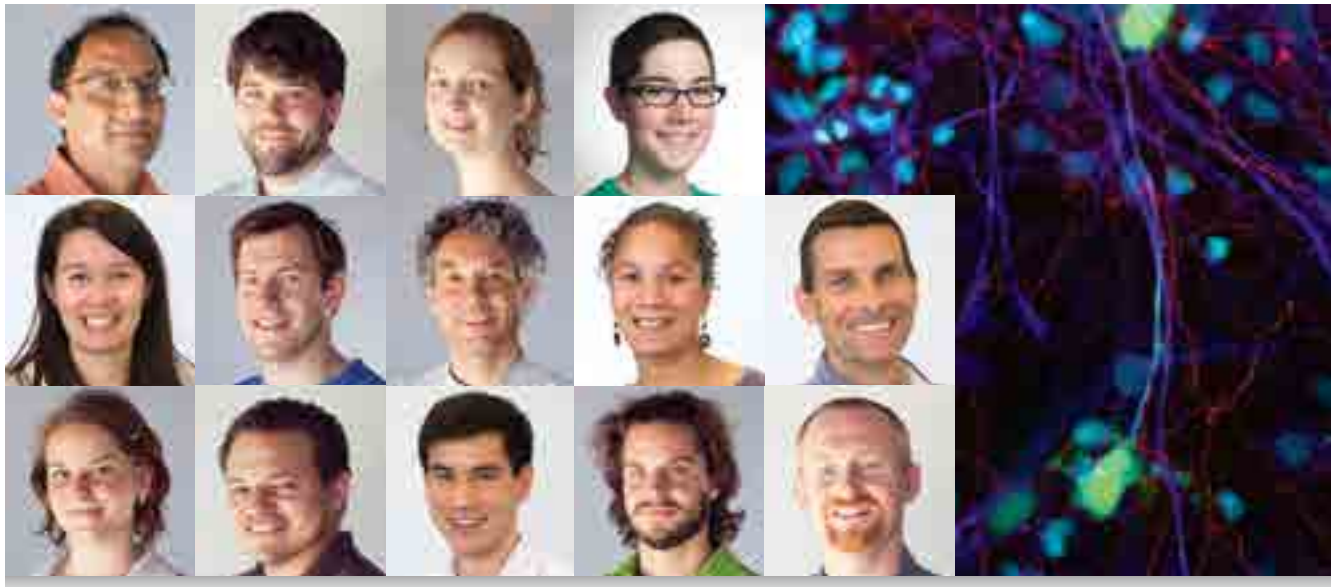
Prior to birth, nerve cells form long processes called axons that connect to other neurons creating functional circuits in the brain. Researchers in the Richards laboratory are studying how the brain forms these connections during development.

This year, the laboratory's work in the area of callosal axon targeting was published in the journals *Cerebral Cortex* and *Developmental Biology*. This work demonstrated a role for the axonal guidance molecules Slit, Robo, Netrin and DCC in the formation of the corpus callosum and provided new insight into how these different families of molecules may interact in correct guidance.

Work with collaborators in the USA and Canada on human brain development and the function of KCC3, a gene involved in a congenital brain disorder called Andermann syndrome, was published in *The Journal of Neuroscience*.

Also in 2012, two students graduated from the PhD program, Ilan Gobius and Sharon Mason. Both students received excellent reviews of their theses. A third PhD student, Sha Liu will finalise her thesis in 2013. Three new PhD students joined the laboratory in 2012, Laura Fenlon, Gonzalo Almarza and Amelia Douglass. Amelia is completing her PhD jointly with Professor Rüdiger Klein at the Max Planck Institute in Munich. Two new Bachelor of Science Honours students, Laura Morcom and Jonathan Lim, will complete projects in 2013.

This year Dr Rodrigo Suárez received a fully funded scholarship to attend a course on Neural Systems and Behaviour at the Instituto de Ciências Biomédicas da Universidade de São Paulo, Marine Biological Laboratory. Gonzalo Almarza received a scholarship to attend a course in Molecular Anatomy at Okinawa Institute of Science and Technology, organised by the Allen Brain Institute.



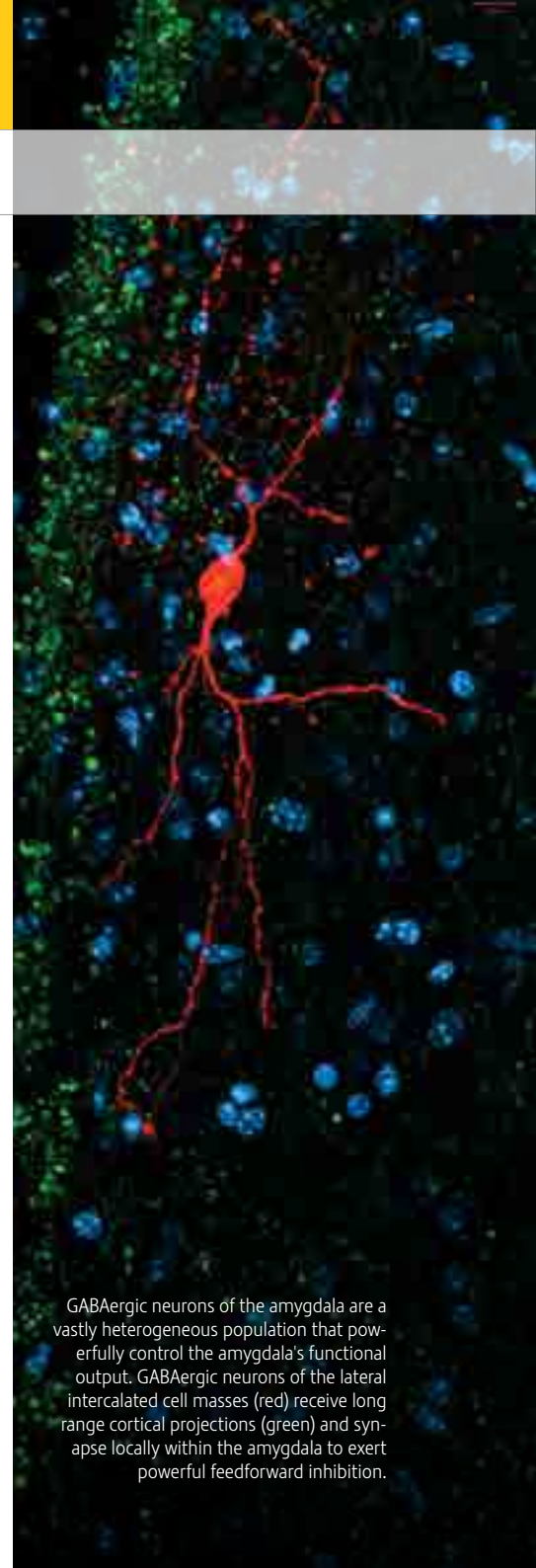
2012 Laboratory Members L-R: Pankaj Sah, Peter Curby, Christine Dixon, Helen Gooch, Sarah Hunt, Roger Marek, John Morris, Margreet Ridder, Peter Stratton, Cornelia Strobel, Robert Sullivan, Tim Tattersall, Fabrice Turpin, Francois Windels. *Not pictured:* Eleanora Autuori, Sepideh Keshavarzi, Christopher Nolan, Petra Sedlak, Li Xu. **Background:** Glial processes (dark blue) make a web that bridges together islands of neurons (nuclei labelled pale blue) and a network of interconnecting fibres (red). Image Robert Sullivan.

Mechanisms that underpin learning and memory formation

One of the major goals in neuroscience today is to understand the mechanisms that underlie learning and memory formation. This information is a prerequisite not only for understanding the biology of mind but also for the discovery of therapies that can alleviate disorders such as anxiety, depression and stress. The Sah laboratory studies the physiological and molecular mechanisms that underlie learning and memory formation. To achieve these goals it focusses on a part of the brain called the amygdala. The amygdala is an almond shaped structure in the mid temporal lobe that is responsible for assigning emotional salience to sensory stimuli. In particular, it is involved in a simple learning paradigm – fear conditioning – that involves the rapid and long lasting acquisition of 'emotional' memories. Moreover, the amygdala is involved in emotional processing and neural circuit dysfunction in the amygdala is thought to underlie a range of anxiety disorders such as general anxiety and post-traumatic stress disorder. Understanding the mechanisms that underlie fear-related learning is therefore most likely to yield a mechanistic understanding of the biology of learning and storage of emotional memory, and why changes in these circuits lead to anxiety disorders. The group uses a combination of electrophysiological recording, calcium imaging, molecular analysis, anatomical reconstruction and behavioural studies to understand the circuitry of the amygdala, how activity in these circuits results in learning, and why its dysfunction causes anxiety disorders.

In collaboration with Professor Joe Lynch, the group is exploring the molecular identity of receptors in the amygdala that could be targets for the development of new anxiolytic drugs.

The team has also established a a collaboration with Professor Peter Silburn (UQ Centre for Clinical Research) to study neural activity in the human brain. These recordings are revealing how the human brain processes information and how it changes in disease.



GABAergic neurons of the amygdala are a vastly heterogeneous population that powerfully control the amygdala's functional output. GABAergic neurons of the lateral intercalated cell masses (red) receive long range cortical projections (green) and synapse locally within the amygdala to exert powerful feedforward inhibition.

Laboratory Head **Professor Mandyam Srinivasan**

2012 Laboratory Members L-R: Mandyam Srinivasan, Kathy Asmussen, Samuel Baker, Brenda Campbell, Julia Groening, Michael Knight, Nikolai Liebsch, Laura McLeod, Ingo Schiffner, Dean Soccol, Saul Thurrowgood, Hong Vo. *Not pictured:* Aymeric Denuelle, Richard Moore, Gavin Taylor, Trevor Weatherhead, William Warhurst. **Background:** Image captured by the vision system of an experimental aircraft executing autonomous flight and mapping its trajectory on the ground.

Visual guidance in insects and birds, and aircraft navigation systems

Flying insects display remarkable visual agility, despite their diminutive brains. The Srinivasan laboratory is using honeybees and budgerigars as models to understand how vision guides flight and enables navigation. They are also using these insights to design novel, biologically inspired strategies for the guidance of aircraft.

Honeybees are visually agile flying machines, avoiding collisions with stationary obstacles as well as other flying insects. The Srinivasan team has recently demonstrated that bees indeed use simple rules, based on specific visual cues, to avoid mid-air collisions with other bees. Some of these findings are of potential relevance to aviation safety.

How do birds fly rapidly and safely through dense foliage? Members of the Srinivasan team have examined how budgerigars fly through narrow gaps. The results are revealing that these birds possess individual 'body images' that enable them to know in advance whether a gap can be traversed safely, and whether the wings need to be tucked in to achieve a safe passage. Other studies are showing that birds are 'handed' just like humans, but handedness in birds varies from individual to individual, unlike humans who tend to be mostly right-handed. This unpredictable feature has important implications for their evolution and social behaviour.

In the area of robotics, other members of the group have developed and successfully tested algorithms for a vision system that uses information from the sky to estimate heading direction, as well as the direction of the prevailing wind. These algorithms can be used to compensate for winds in long-range navigation as well as during landing and take off. Work is underway to port many of the guidance algorithms that the group has developed over the past five years to our new, highly manoeuvrable multi-rotor aircraft.

Sequential images of a budgerigar flying through a tunnel in an experiment to investigate how birds fly safely through narrow passages.

Professor Mandyam Srinivasan holds a joint appointment with the School of Information Technology and Electrical Engineering.

Laboratory Head **Associate Professor Bruno van Swinderen**

2012 Laboratory Members L-R: Bruno van Swinderen, Ben Calcagno, Leonie Kirszenblat, Ben Kottler, Angelique Paulk, Jacqui Stacey, Michael Troup, Bart van Alphen, Melvyn Yap, Oressia Zalucki, Yangqiong Zhou. **Background:** Dr Bart van Alphen working in the van Swinderen laboratory.

Perception and cognition in *Drosophila*

The van Swinderen laboratory uses the fruit fly model *Drosophila melanogaster* to investigate perception and cognition. By combining powerful molecular genetic tools with high-throughput behavioural assays and electrophysiology, the group is able to study the underpinnings of complex phenomena such as selective attention, memory, general anaesthesia, and sleep in the more simple fly brain. To pay attention, learn and sleep a brain must be able to suppress parts of the outside world effectively. Understanding how this suppression mechanism works is a central question of the laboratory, with a focus on visual systems.

Using high-throughput behavioural assays, the laboratory has developed a model for studying attention-like defects in a fly model for schizophrenia. This research, done in collaboration with the laboratory of Associate Professor Darryl Eyles, revealed a role for developmental dopamine in modulating visual attention in adult animals. Brain recording experiments in behaving flies in virtual reality environments revealed attention-like switching dynamics in the fly brain, which can now be measured to understand how molecules such as dopamine guide behavioural choices in healthy animals as well as in disease models.

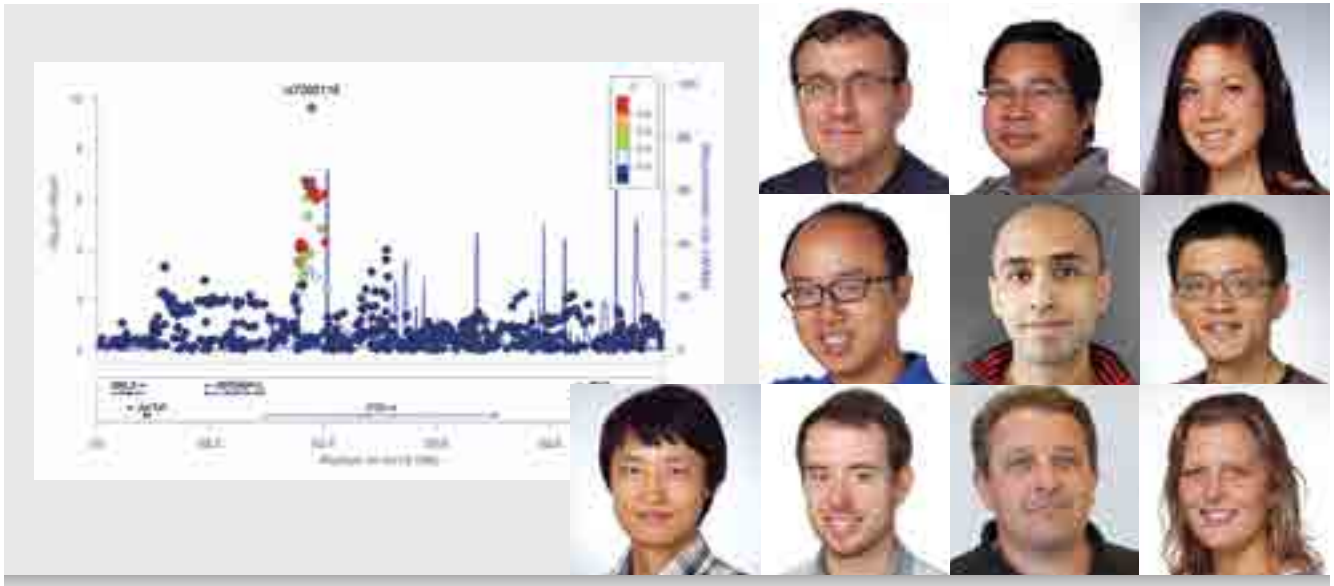
In collaboration with colleagues in Beijing and the USA, the laboratory is also focussing on a population of neurons in the fly's central brain thought to be involved in sleep regulation as well as visual learning and memory. Convergence of behavioural effects stemming from activity of these central neurons is being studied by behavioural genetics and electrophysiology.

In addition to *Drosophila* work, the laboratory also studies the honeybee in order to gain insight into neural activity associated with visual attention and learning. The honeybee offers valuable behavioural repertoires and a larger brain to complement similar questions addressed in the fruit fly.

A *Drosophila* moving through the natural world will run into the same problems we do, however, they do it with a fraction of the number of neurons we do. How do they do it? Image Angelique Paulk.

Laboratory Head **Professor Peter Visscher**

Part of the Eureka prize finalists team. The team was shortlisted in recognition of their work showing that genetic risk for complex diseases such as schizophrenia is due to the cumulative effect of hundreds or thousands of genes. Clockwise from top: Professor Peter Visscher, Dr Jian Yang, Associate Professor Naomi Wray. Not pictured: Dr Hong Lee and Professor Mike Goddard from the University of Melbourne.



2012 Laboratory Members L-R: Peter Visscher, Beben Benyamin, Marie-Jo Brion, Guo-Bo Chen, Gibran Hemani, Jian Yang, Hong Lee, Gerhard Moser, Joseph Powell, Anna Vinkhuyzen. *Not pictured:* Allan McRae, Konstantin Shakhbazov, **Background:** A variant in the FTO gene is associated with increased variability in body mass index (BMI). BMI at midlife is associated with risk of dementia.

Finding genes for common diseases & their risk factors in human populations

The Visscher laboratory specialises in quantitative and statistical genetics, population genetics, human genetics and bioinformatics, with the ultimate aim of trying to understand the genetic basis of differences in risk to disease and other phenotypes between individuals. The group uses theoretical derivations, simulation studies, development of new analytical methods and software tools, and the application of advanced statistical analysis methods to genetic and phenotypic data.

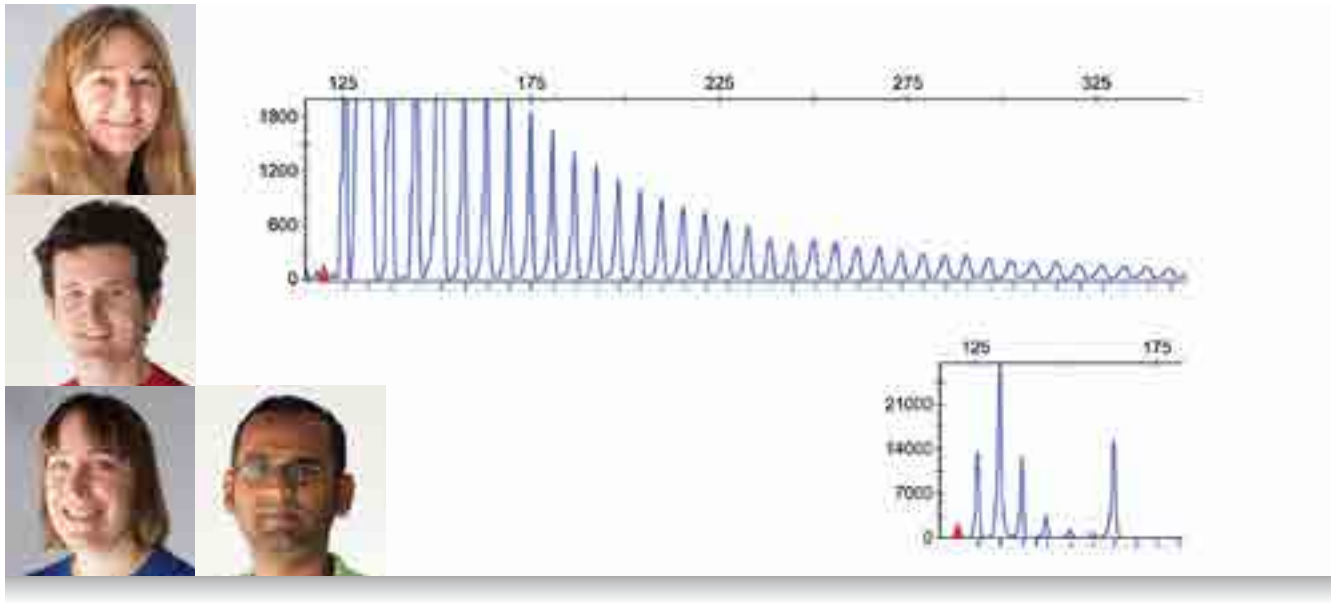
In 2012, using innovative statistical methods, the group demonstrated that complex traits, such as height, body mass index, behaviour, cognitive ability and some common diseases, are caused by the cumulative effect of hundreds of genes. In addition to a number of significant publications, this also resulted in a team led by Professor Visscher being shortlisted for the 2012 Eureka Prize in the category of Scientific Research.

The group has also contributed analysis expertise to a large number of international research consortia that have found genes affecting endometriosis, schizophrenia, asthma, circulating lipid levels, red blood cell formation, rheumatoid arthritis and stature.

The group has developed widely used statistical methods and software to estimate the effects of genes, chromosomes and the whole genome on disease susceptibility. In data applications it has been demonstrated that genetic variation in childhood and adult cognitive ability can be captured by DNA markers. This work is the continuation of a long-standing collaboration with Professor Ian Deary from the University of Edinburgh.

In collaboration with researchers from the Queensland Institute of Medical Research, Professor Visscher has established the Brisbane Systems Genetics Study, with the aim of understanding genetic variation in gene expression and its correlation with individual differences in complex traits. They have shown that gene expression itself is under genetic control, and that this control is tissue specific.

Professor Peter Visscher holds a joint appointment with the UQ Diamantina Institute.



2012 Laboratory Members L-R: Robyn Wallace, Tim Butler, Marie Mangelsdorf, Ramesh Narayanan. *Not pictured:* Hinson Li. **Background:** In 2011 a mutation in the C9orf72 gene was found to be the largest known cause of MND. The gene contains a 6 base pair repeat (GGGGCC). The figure shows an analysis of repeat copy numbers. Each peak represents one copy of the repeat. Controls (bottom) have between 2 and 30 copies of the repeat. In some MND patients the number of repeats increases to up to 2000 copies (top).

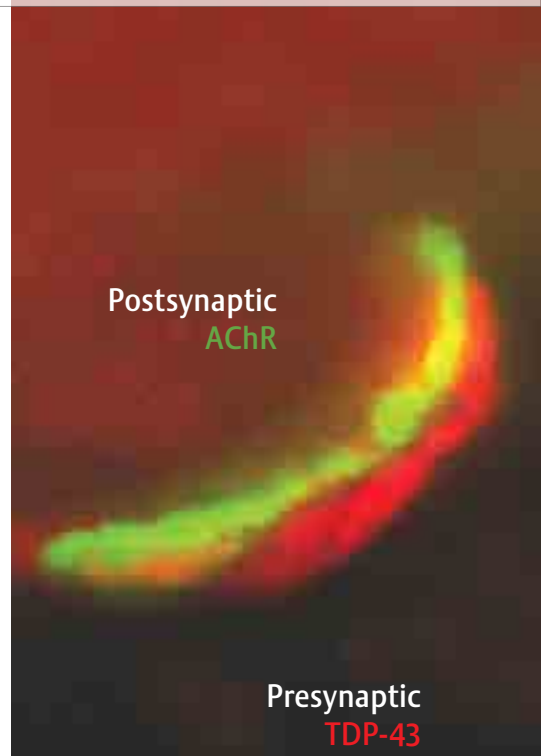
Understanding the mechanisms of motor neuron disease

The main focus of the Wallace laboratory is the genetics and molecular mechanisms of motor neuron disease (MND). MND is a rare, incurable disorder with late onset. Although most MND cases are not inherited, a small percentage are due to genetic mutations. The group is using advanced genomic techniques to understand how these genes cause MND and to test potential treatments.

Several of the known MND genes encode proteins involved in gene regulation. The group is studying one of these proteins, TDP-43. The function of TDP-43 in the nervous system is currently unknown and its role in the pathogenesis of MND remains unclear. In 2012 the Wallace laboratory published a report in which they used RNA immunoprecipitation to identify mRNAs to which TDP-43 binds. The TDP-43 targets were found to include a large number of genes involved in synaptic activity. Additionally, TDP-43 was found at the neuromuscular junction (NMJ), one of the earliest sites of pathology in MND patients. This has led to the hypothesis that TDP-43 may regulate RNA transport in axons to the NMJ for local translation. The team is now collaborating with the Hilliard group to study TDP-43-mediated RNA transport in *Caenorhabditis elegans* neurons to determine the role of this cellular process in MND pathology.

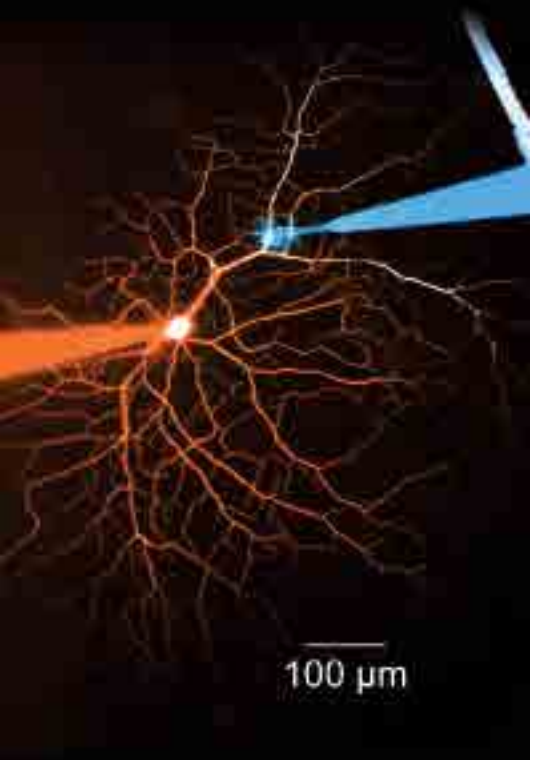
RNA binding proteins, including TDP-43, are also known to regulate alternative splicing of pre-mRNAs. The team is studying alternative splicing defects in a mouse model of MND using exon microarrays. A number of genes have been found in which aberrant splicing occurs in both brain and spinal cord mRNAs compared to a normal mouse. For several genes, the mis-splicing occurs prior to the onset of MND symptoms. These genes have the potential to become biomarkers of disease progression in patients with MND.

Potential outcomes of these projects include crucial insight into understanding how motor neurons degenerate in MND and the identification of novel therapeutic targets.

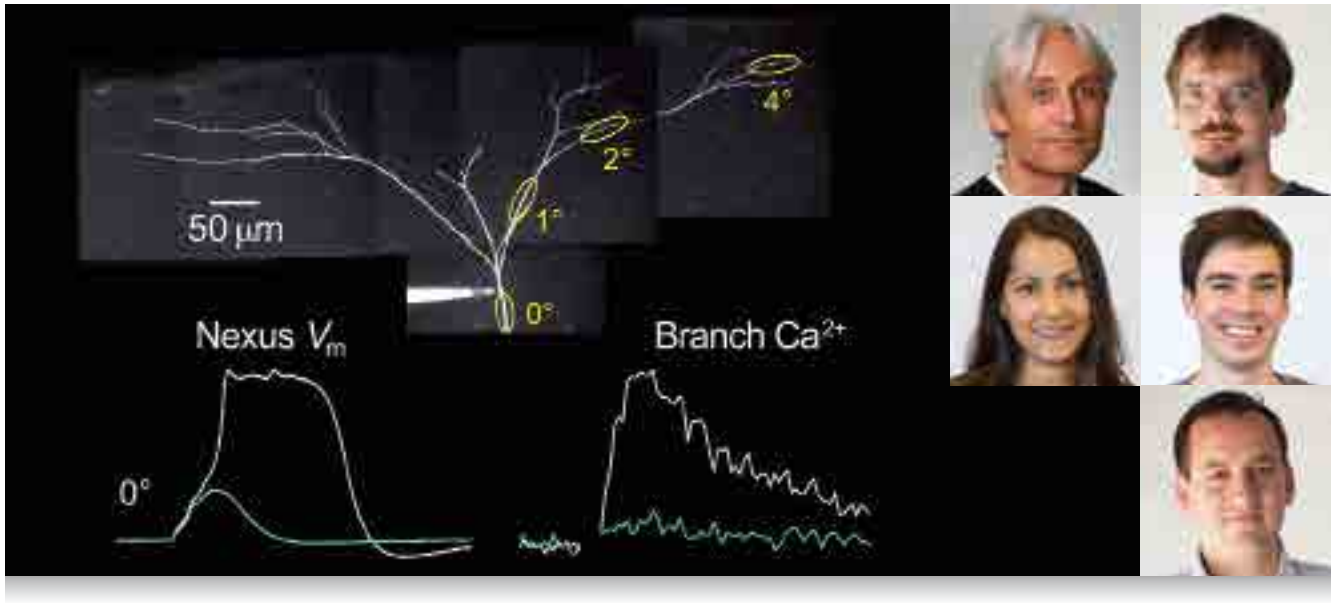


Immunohistocytochemistry of the mouse neuromuscular junction shows the presence of TDP-43 (red) at the presynaptic terminal and acetylcholine receptors (AChr) on the postsynaptic muscle terminal (green). Image Associate Professor Peter Noakes, School of Biomedical Sciences.

Laboratory Head **Associate Professor Stephen Williams**



Simultaeous whole-cell recordings from a retinal ganglion cell.



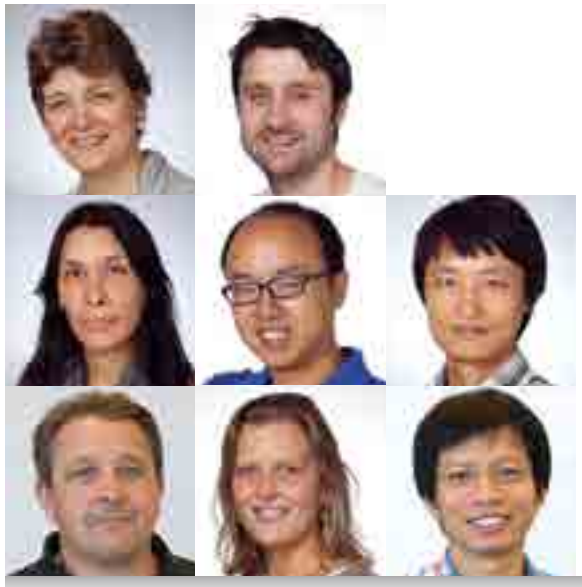
2012 Laboratory Members L-R: Stephen Williams, Arne Brombas, Florence Cotel, Lee Fletcher, Ben Sivyer.
Background: Dendritic activity recorded from a layer 5 neocortical pyramidal neuron.

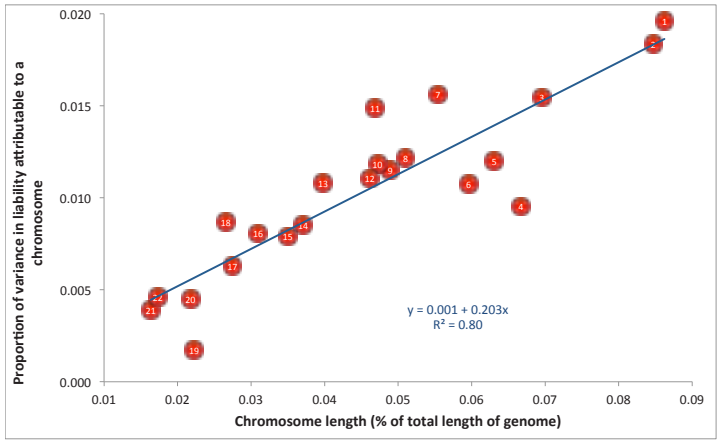
Computation in neurons and circuits

The Williams laboratory is investigating how single neurons and circuits of neurons carry out computations that ultimately control behaviour. Using advanced electrophysiological and optical techniques, the group is investigating how neurons integrate input signals, termed synaptic potentials, received throughout their dendritic tree. Work has shown that synaptic inputs received at defined areas of the dendritic tree uniquely control the output of neurons. The laboratory seeks to understand the rules and mechanisms that form and control this rich integrative process and explore the relevance of active dendritic synaptic integration to the operation of neuronal networks.

Recent work has revealed that active dendritic integration is recruited by physiological stimuli and implements circuit based computations in the neocortex and retina. Researchers have discovered that dendritic processing implements multi-modal processing in neocortical circuits, acting to compute the location of objects in the environment by the integration of motor and sensory information. In the output neurons of the retina, members of the Williams laboratory have found that dendritic integration underlies the computation of image motion. The computation of the direction of image motion was found to be mediated by the inhibitory synaptic control of a cascade of active dendritic integration compartments that are activated by light stimuli. Taken together these findings reveal that active dendritic integration is a key component of neuronal circuit operation. This work will enable neuroscientists to better understand how networks of neurons function and ultimately how these processes are disturbed in disease.

In 2012, Associate Professor Williams was a co-organiser of an international conference on dendrites, held in the USA.





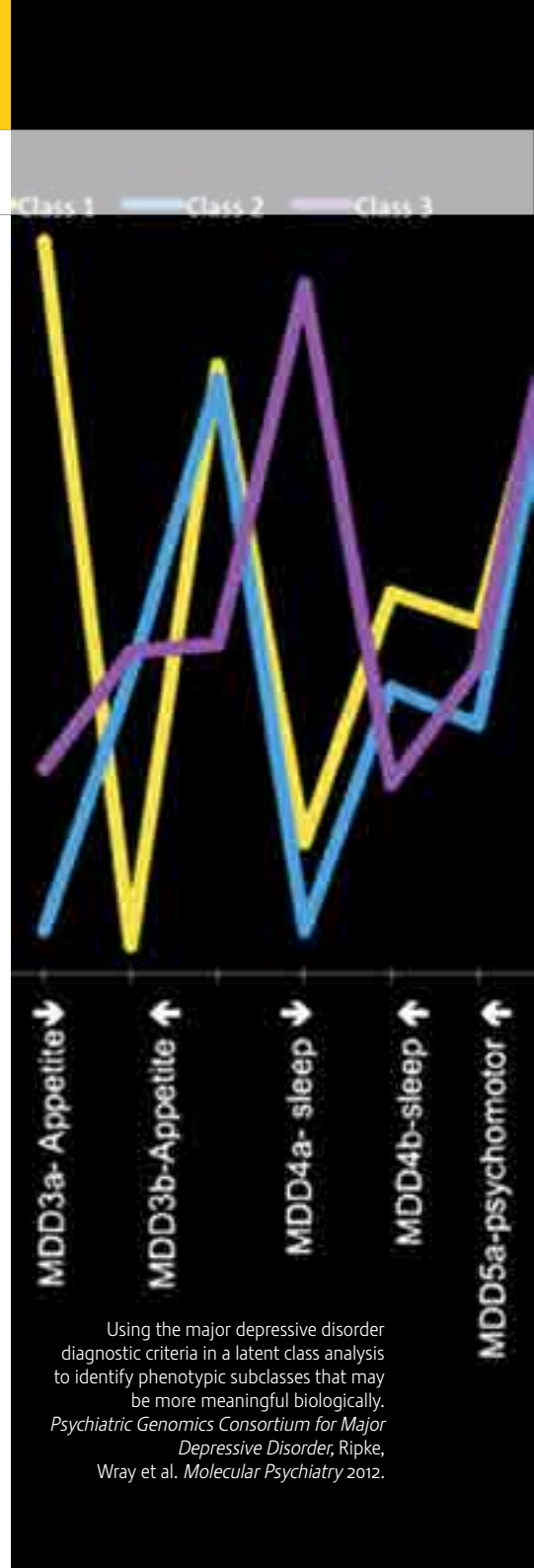
2012 Laboratory Members, L-R: Naomi Wray, Enda Byrne, Tania Carillo-Roa, Guo-Bo Chen, Hong Lee, Gerhard Moser, Anna Vinkhuyzen, Haoyu Zhang. QBI Bioinformatics Core: Qiongyi Zhao. *Not pictured:* Andreas Lunderg, Haoyu Zhang, Zong-Hong Zhang. **Background:** Direct evidence for the polygenic nature of schizophrenia. The variance in liability is attributed to each chromosome and reflects the length of the chromosome. The points are labelled by chromosome number. Lee et al. *Nature Genetics* 2012.

Statistical probing of the genomic complexity of psychiatric disorders

Research in the Wray laboratory focusses on understanding the genetic contribution to psychiatric disorders. The group specialises in the development of new analytical methods and the application of advanced statistical methods to the analysis of genetic and phenotypic data of psychiatric disorders. They play a leading role in the international Psychiatric Genomics Consortium that has brought together large samples of cases and controls of five psychiatric disorders: schizophrenia, bipolar disorder, major depressive disorder, attention deficit hyperactivity disorder and autism spectrum disorder. In 2012, the Wray laboratory published a novel analysis of the consortium's schizophrenia data in *Nature Genetics*. The genetic architecture of schizophrenia (i.e. the number of genetic variants and their contribution to risk) has been a subject of much debate and controversy in the field. Analyses of the Wray laboratory provided empirical support of a highly polygenic architecture. These results will help guide future research designed to identify individual risk variants and biological pathways that underpin human disease.

In 2012, the Wray laboratory published new methods that use genome-wide markers to interrogate the shared genetic relationship between psychiatric disorders. The methods use sets of unrelated cases and controls from two disorders, but based on the old adage "we are all related", searches the genome for variants more likely to be shared in cases of different diagnostic classes. The methods are currently being applied to the five major disorders of the Psychiatric Genomics Consortium. Research has also focussed on strategies that define more homogenous diagnostic classes for genetic studies of psychiatric disorders, for example using major depression, postnatal depression or sleep dysregulation.

Members of the Wray laboratory were also part of a team that were finalists for a 2012 Eureka Prize in the category of Scientific Research.



Using the major depressive disorder diagnostic criteria in a latent class analysis to identify phenotypic subclasses that may be more meaningful biologically. *Psychiatric Genomics Consortium for Major Depressive Disorder*, Ripke, Wray et al. *Molecular Psychiatry* 2012.

Senior research assistant Nancy Malintan in the Meunier laboratory.

Centre for Ageing Dementia Research

Housed within the QBI, the Centre for Ageing Dementia Research (CADR) is Australia's first and only facility focussed entirely on research into the prevention and treatment of dementia.

In February 2012, Professor Jürgen Götz was appointed Foundation Chair of Dementia Research at UQ and inaugural Director of CADR.

Against a backdrop of Australia's maturing population, ageing dementia is emerging as one of the country's most pressing health problems.

The disorder affects more than 320,000 Australians and is the nation's third leading cause of death, after heart disease and stroke. There is no cure.

Without a significant medical breakthrough, the number of Australians living with dementia is expected to soar to over one million by 2050.

The CADR team has already made discoveries that are leading to the development of tools to prevent onset, or slow the progression of dementia.

Along with early detection and preventative strategies, therapeutic intervention is key to minimising the social and economic impact of dementia in Australia.

The aims of CADR are:

- To uncover basic disease mechanisms and use this information for therapeutic intervention
- To understand the normal role of genes and proteins implicated in diseases such as Alzheimer's and frontotemporal dementia
- To develop new pharmaceuticals to promote new nerve cell production to prevent or delay the onset of ageing dementia, and to delay its progression
- To develop new pharmaceuticals to prevent brain nerve cells from dying or degenerating during ageing
- To develop low-cost, non-pharmaceutical therapies to prevent or delay the onset of ageing dementia, and to delay its progression
- To develop novel diagnostic and therapeutic antibodies as well as methods to make the blood-brain barrier, a major obstacle in drug delivery, penetrable to therapeutic molecules.

About Professor Götz

A world-leader in Alzheimer's disease research, Professor Götz has made several ground-breaking discoveries, including work published in the prestigious journals *Science* and *Cell*, that brought to light the molecular mechanisms underlying the loss of brain function in Alzheimer's disease.

Professor Götz has earned international acclaim for the discovery of how the molecule TAU causes neuronal death in Alzheimer's disease.

His insights have been used toward developing new therapeutic approaches for dementia treatment.

The current prescribed drugs provide symptomatic treatment, without halting the progressive neurodegeneration and nerve cell loss that characterises the Alzheimer's brain.

Professor Götz and his team use animal models as they not only help in understanding what goes awry in the Alzheimer's brain, they are also essential tools in developing tailored therapies.

Professor Götz and his team continue to develop and improve a diverse array of strategies aimed at curing the pathology of Alzheimer's disease.

The molecular entities include small molecules, such as sodium selenate, which is currently being tested in a clinical trial, as well as antibodies to target proteins in the brain, an organ long thought to be immunoprivileged and hence not accessible to vaccination strategies.

The research team is currently refining these strategies to make them ultimately applicable to humans, and is optimising methods to penetrate the blood-brain barrier for drug delivery.

CADR scientists are on the trajectory to continue to make discoveries that help the growing number of dementia patients, both in Australia and overseas.

Centre for Ageing Dementia Research

Profile

Dr Victor Anggono, Centre for Ageing Dementia Research

Efficient communication between neurons is crucial for all brain activity and depends on the ability of neurons to transmit chemical signals (neurotransmitters) from the so-called presynaptic nerve terminals to postsynaptic receptors on other neurons. Years of research has shown that dysregulation of neurotransmitter release and aberrant movement of postsynaptic receptors lead to impairment in neuronal communication and deficits in social behaviour, learning and memory in mice. There is also considerable evidence to suggest that synapses, the specialised structures through which neurons transmit and receive signals, are particularly vulnerable in Alzheimer's disease, establishing synaptic dysfunction as one of the earliest events in the pathogenesis of Alzheimer's disease prior to neuronal loss.

The overall goal of Dr Anggono's research is to unravel the cellular and molecular mechanisms of neuronal communication, in order to understand physiological phenomena such as learning, memory, behaviour and disease. In the past few years, his team has been working on the protein syndapin, which plays an important role in neuronal signalling and has the ability to bind, sense and generate curvature on the plasma membrane. Dr Anggono and his collaborator, Professor Phillip Robinson at the University of Sydney have found two novel phosphorylation sites on the syndapin lipid binding domain that regulate the ability of syndapin to bind and tubulate the lipid membrane. Mutations in either of these two phosphorylation sites impair the ability of a neuron to extend its processes. In addition, Dr Anggono also led a project that involves groups of researchers from The Johns Hopkins University, USA, and the University of Cologne, Germany, examining a novel role for syndapin in regulating cerebellar long-term depression, thought to be important in controlling fine-motor movement. More recently, his team has collaborated with Professor Jürgen Götz to investigate the underlying mechanisms responsible for the loss of synaptic proteins in mouse models of Alzheimer's disease.

Above: Widespread accumulation of hyperphosphorylated protein aggregates in a mouse model of Alzheimer's disease. Far left: Professor Jürgen Götz. Right: Dr Victor Anggono.

Science of Learning Centre

The Science of Learning Centre (SoLC), the first centre of its kind in Australia, brings together expertise in neuroscience, cognitive psychology and education to translate cutting-edge neuroscience into effective, efficient and practical teaching techniques for application in the classroom and workplace.

"Understanding the neural mechanisms of learning has a huge potential to impact on the practice of education. Every change in behaviour that results from learning can be traced back to a change in our brain," said SoLC Co-Director Professor Pankaj Sah.

Insights into complex neural circuitry, whole-brain activity and the interaction between memory systems, emotion and attention have led to new techniques for assisting people with learning difficulties in areas such as numeracy and literacy.

"We also started from a strong base in existing teaching practices, and when this experience is integrated with foundational research into the biological mechanisms of learning, many new possibilities exist for improving and widening the impact of successful practices," added Co-Director Professor Ottmar Lipp.

One new project, which commenced this year, is an investigation into automaticity and attention. As we develop proficiency in a new task, the load on our short-term working memory decreases and we are able to rely more and more on automatic processes. This automatic processing occurs for example, when we drive a car.

Neuroscientist Associate Professor Bruno van Swinderen is using simple navigational tasks for honey bees and observing the interplay between the bee's attention and motor system, as the task is made harder. The research is showing how working memory impacts on the motor system in bees.

Meanwhile, cognitive psychologist Associate Professor Ross Cunnington and Dr Robert Colvin are developing the navigational task for human experiments, to establish transferal of the underlying learning principles and to understand the important trade-off between attention and automaticity.

Outcomes from this research will provide guidance in planning the length of learning activities, determining when learning ceases and automaticity kicks in for repetition based activities such as spelling words.

Joint Sino-Australian Neurogenetics Laboratory

The Joint Sino-Australian Neurogenetics Laboratory, an initiative of QBI, UQ's Diamantina Institute and the Second Military Medical University (SMMU) in Shanghai, is dedicated to exploring how genes influence brain development and function, and focusses on discovering the genes that cause or make individuals susceptible to certain neurological and mental illnesses.

Under the guidance of Professor Huji Xu, who holds an appointment with QBI and SMMU, researchers are probing the neurogenetics of motor neuron disease (MND), schizophrenia, stroke and epilepsy.

Researchers in the laboratory are engaging with a network of neurologists and psychiatrists at various hospitals and universities across China to study ethnically remote populations. It is anticipated that differences in ancestral genetic diversity will enable mapping of genes in certain populations that are not easily identified in other populations.

Project profile

Neurogenetics of motor neuron disease

MND is a devastating neurodegenerative disease characterised by progressive muscle weakness and wasting. About 10 per cent of MND is familial, that is more than one person in the family has been or is affected, and is usually the result of a genetic mutation. Genetic mutations are also found in cases where there is no family history – sporadic cases.

QBI's Professors Perry Bartlett and Peter Visscher, in collaboration with Professor Matt Brown from the UQ Diamantina Institute and Professor Huji Xu from the SMMU, are conducting large population studies to identify genes that are associated with MND. This research will lead to new genetic markers, aid development of diagnostic tools and identify new therapeutic targets for MND.

Above: UQ's Vice-Chancellor Professor Peter Høj meets with staff at the Second Military Medical University in Shanghai. Below: Researcher Dr Marie Mangelsdorf in the joint laboratory at QBI.

Joint Laboratory of Neuroscience and Cognition

The Joint Laboratory of Neuroscience and Cognition between the Chinese Academy of Sciences' Institute of Biophysics in Beijing and QBI, headed by Professor Perry Bartlett (QBI) and Professor Rongqiao He (IBP) continues to develop, with collaborations between the two organisations strengthening and expanding.

In July QBI was fortunate to host the President of the Chinese Academy of Sciences, Professor Chunli Bai. Professor Bai is extremely supportive of the research collaboration between the two organisations.

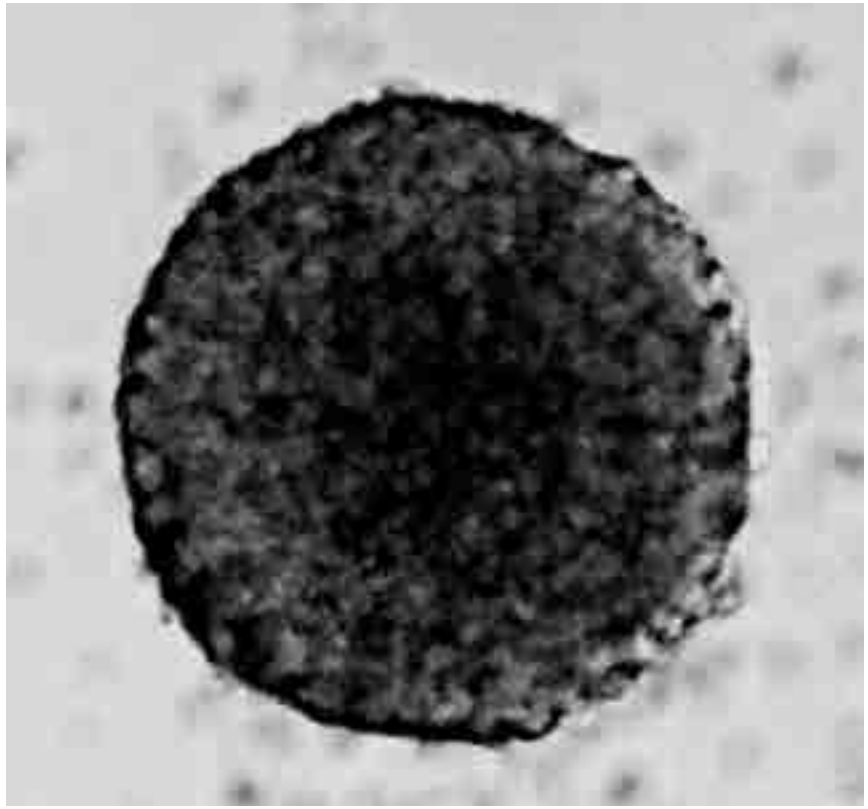
There are now over 20 researchers working across five projects within the Joint Laboratory in Beijing and Queensland, united in the quest to identify the key mechanisms that regulate brain plasticity, and to translate this understanding into promoting normal function and ameliorating disease.

To ensure the ongoing success of the Joint Laboratory Associate Professor Yajing (Maggie) Sun was appointed as Liaison Manager. Among other duties, Associate Professor Sun will manage liaisons with Chinese hospitals for clinical research and explore commercial opportunities in China.

Project profile

Uncovering the origins of pain

The amygdala, with its role in emotional processing and the target region of nociceptive fibres of the parabrachial area, has been proposed to be the site of integration for painful sensations and affective responses. Professor Pankaj Sah (QBI) has combined his knowledge of amygdala physiology with Professor Jianyuan Sun's (IBP) expertise in presynaptic recordings of the Calyx of Held to directly record from large parabrachial presynaptic basket terminals, which carry nociceptive information and target central lateral amygdala neurons. This collaborative work is providing a better understanding of these synapses. This will improve our knowledge of how painful information can negatively influence emotions, which can, in severe circumstances such as chronic pain, lead to anxiety and depression. Dr Cornelia Strobel, from Professor Sah's laboratory, spent 6 months working in Beijing with Professor Sun, which followed a visit to QBI from Professor Sun's PhD student Qianwen Zhu in 2011.



Above: An example of a large neurosphere observed in the hypomagnetic field (HMF), from postnatal day 2 mouse subventricular zone tissue. A HMF system in IBP has been upgraded with an advanced magnetic field compensating system and a video monitoring system to investigate the responses of neural stem cells in the mice.

This page: Honours student,
Nika Mohannak in the Meunier laboratory.

Students

Attracted by the Queensland Brain Institute's outstanding reputation, students play an integral role in the cutting-edge research undertaken at the Institute. A mix of local students and international students from as far afield as China, Latin-America and Europe brings fresh, innovative and international approaches to QBI's neuroscience research.

In 2012, QBI had a total of 81 research higher degree students enrolled, 17 of whom were international candidates from Austria, Canada, Chile, China, France, Germany, India, Iran, Korea, Malaysia, Myanmar, New Zealand, Norway, Singapore, Switzerland, Taiwan, Thailand, the United Kingdom, the United States of America and Vietnam.

QBI welcomed 33 new domestic and international students who commenced their research candidature during the year. QBI was also delighted to see the conferral of 13 PhD awards upon the following students across two graduation ceremonies held in July and December and would like to congratulate: Conor Champ (Marshall laboratory), Claire Foldi (Eyles/Burne laboratory), Clare Giacomantonio (Goodhill laboratory), Ilan Gobius (Richards laboratory), Lauren Harms (Burne laboratory), Sharon Mason (Richards laboratory), Linda May (Coulson laboratory), Richard Moore (Srinivasan laboratory), Sumiti Saharan (Bartlett laboratory), Hugh Simpson (Goodhill laboratory), Cornelia Strobel (Sah laboratory), Nancy Malintan (Meunier laboratory), and Qian Wang (Lynch laboratory). An MPhil was awarded to Haley Cox (Cooper laboratory). These graduates have subsequently gone on to postdoctoral work or into research administration.

Multiple highly competitive scholarships were awarded to QBI students during the year. Some of the most successful international scholarship recipients were: Stephanie Biergans (Germany) who was awarded the top international scholarship offered at UQ, the International Postgraduate Research Scholarship (IPRS), in conjunction with UQ Centennial Living Allowance and the UQ Advantage Top-Up. Thanh Nguyen (Vietnam) and Xianfeng Yang (China) were both awarded the IPRS while also receiving UQ Centennial Living Allowances and QBI Top-Up Scholarships. French PhD student Aymeric Denuelle was awarded the IPRS, UQ Centennial Living Allowance, and a scholarship from the Commonwealth Scientific and Industrial Research Organisation (CSIRO). Fourteen domestic PhD students who commenced their studies in 2012 each secured the top Australian Government scholarship, the Australian Postgraduate Award (APA). Domestic PhD students Lee Fletcher and Zoran Boskovic were both successful in securing an APA and a UQ Advantage Top-Up Scholarship for their research into synaptic integration, and adult forebrain function, respectively.

QBI also welcomed undergraduate and postgraduate coursework students through the annual UQ Summer Research Program, and for the first time in 2012, the UQ Winter Research Program. For the Summer Research Program 2012, QBI received 22 domestic and international undergraduate students to undertake a range of projects across 14 different laboratory groups within QBI. The inaugural Winter Research Program involved a total of five students who participated in various laboratory-based projects over a six-week period.

Students chart course to success

Students at QBI are provided with opportunities to pursue their research interests, while working closely with dedicated neuroscientists. This research and work experience provides the students with a solid foundation for career success.

Dr Richard Moore

Dr Richard Moore joined QBI's bio-robotics laboratory, headed by Professor Mandyam Srinivasan, in June 2008 to investigate novel vision-based guidance systems for autonomous aircraft. Richard's research was focussed on developing computationally lightweight and robust guidance and navigation algorithms for small-scale unmanned aircraft by taking inspiration from the principles by which many winged insects stabilise their flight and navigate. One of the key outcomes from his research was the demonstration of complex flight behaviours, such as autonomous return-to-base and landing, for the first time using only visual information and on-board computing resources.

After receiving his PhD from UQ in late 2012, Richard secured a Postdoctoral Fellowship with the School of Engineering and Applied Sciences at Harvard University where he is applying his knowledge of bio-inspired visual guidance systems to the design of the Robbie – an insect-sized, flapping-wing, micro aerial vehicle. His research is currently directed towards investigating how swarms of autonomous robotic insects could be used to efficiently explore new environments.

Dr Lauren Harms

Dr Lauren Harms began her doctoral research focussing on brain development in vitamin D deficient mice under the supervision of Dr Thomas Burne and Associate Professor Darryl Eyles early in 2008.

The focus of Lauren's doctoral research was the potential impacts of prenatal vitamin D deficiency on brain development and behaviour with relevance to psychiatric disorders. Lauren's research showed vitamin D deficient mice and control mice displayed differences in the expression of genes involved in developmental processes, some of which are implicated in schizophrenia. In addition, Lauren's research showed an effect on behaviour as the mice aged, demonstrating the long-lasting effect of prenatal vitamin D deficiency. Lauren's research resulted in two first-author papers. Since completing her studies, she has since taken up a postdoctoral position at the University of Newcastle, NSW, where she is continuing to pursue her research interests in animal brain development, with a particular focus on schizophrenia.

Right: Summer student Justin Jin in the laboratory.

MASTER OF NEUROSCIENCE STUDENTS

Master of Neuroscience

The Master of Neuroscience program was introduced in 2010 as an initiative of QBI Director Professor Perry Bartlett and The University of Queensland's Senior Deputy Vice-Chancellor, Professor Deborah Terry, as a pathway for students who wish to shift their career focus to neuroscience and pursue independent research and teaching careers. In 2012, QBI welcomed two new international students and five domestic students into the Master of Neuroscience program: Richard Carey, Matthew Kennett, Elliot Lambert, Kim Loong Lim, Janaina Videra Pinto, Michael Troup and Cameron Turner.

The program is coordinated by QBI and the Faculty of Social and Behavioural Sciences but also spans other centres for neuroscience research at UQ. To ensure quality of student experience and teaching, a quota of 12 students per semester has been imposed upon the course.

Providing research training and core professional skills, the program is a pathway to specialist streams including molecular and cellular neuroscience, neural imaging and computational neuroscience, developmental neurobiology, cognitive and behavioural neuroscience, visual and sensory neuroscience and epigenetics. The Master of Neuroscience runs for three semesters (24 units), although students with Honours or equivalent can complete the program in two semesters (16 units).

In 2012, a total of nine students graduated with the Master of Neuroscience degree. They were Luis Sebastian Contreras Huerta, Kylie Cuthbertson, Laura Fenlon, Gayeshika Leanage, Joel Adams-Bedford, Megan Campbell, Yuan Cao, Athina Eu and Cameron Turner.

Students who have completed their Master of Neuroscience program say that the experience has encouraged them to pursue further study opportunities, such as a PhD.

Compulsory core lecture-based courses in the Master of Neuroscience program are:

- Molecular and Cellular Neuroscience (NEUR7006), which is concerned with cellular and molecular biology of the neuron.
- Systems Neuroscience: Sensory and Motor (NEUR7004) which uses a systems approach to explore the brain with respect to circuits that integrate and process information.
- Cognitive and Behavioural Neuroscience (NEUR7005), which focusses on the elucidation of the neural basis of cognitive and behavioural phenomena.

Together with the three Master of Neuroscience laboratory rotations, which offer 300 hours of supervised practical experience, these courses provide a cohesive introduction to the theoretical and practical aspects of neuroscience. Rotations can be undertaken in a wide number of participating schools, including QBI, UQ's Schools of Psychology, Pharmacy, Medicine, Biomedical Sciences, Microbial and Molecular Biosciences, Information Technology and Electrical Engineering, Perinatal Research Centre, Centre for Clinical Research, the Institute for Molecular Bioscience, Centre for Advanced Imaging and Queensland Institute of Medical Research.

COMMUNITY

Charmaine Paiva is part of the administration team at QBI.

Community

Queensland Brain Institute researchers form an integral part of the communities in which they work and live. They regularly discuss the latest research discoveries with community groups, while also engaging with their peers at scientific conferences.

In 2012, QBI hosted a series of high profile events and conducted a range of community outreach events. In addition to educating Australians about the latest research findings, staff also expanded their efforts to encourage the next generation to consider careers in neuroscience.

ANS meetings

Alongside the Australian Neuroscience Society's Annual Scientific Meeting held on the Gold Coast, researchers from QBI attended a number of satellite meetings.

Bioautism

Held at QBI in January, this meeting focussed on the neural and biological basis of autism spectrum disorders (ASDs). It is estimated that 1 in 100 children are diagnosed with an ASD each year. While the causes of autism are not clear, in recent years significant progress has been made towards unravelling the underlying disease aetiology and candidate mechanisms.

This meeting brought together researchers working on ASDs from multiple disciplines, with the specific goal of addressing how basic and clinical research can accelerate the development of therapies and treatments.

Speakers featured at the meeting included Dr Honey Heussler (Mater Hospital), Dr Natasha Brown (Melb Uni), Dr Peter Enticott (Monash Uni), Dr Jon Brock (Macquarie Uni), Dr Elisa Hill (Melb Uni), Associate Professor Charles Claudianos (QBI, UQ) and Professor David Reutens (CAI, UQ).

Topics discussed included genetics, synaptic and circuit level mechanisms, cognitive mechanisms, animal models, and moving from models and mechanisms to therapeutics.

Cellular and Functional Imaging

This satellite symposium brought together many of the leaders in the field of imaging to present recent results and developments in imaging.

Held at QBI, speakers at the meeting came with extensive experience working on cellular imaging (confocal and multiphoton imaging), whole-field imaging (MRI and PET) as well as optogenetic techniques.

Speakers included QBI's Dr John Power who discussed calcium store release in amygdala neurons. Associate Professor Peter Thorn, School of Biomedial Sciences spoke on real-time imaging exocytosis, and QBI's Professor Pankaj Sah gave insight into the intrinsic circuitry of the amygdala.

Neuronal Polarity in Health and Disease: Role of Cytoskeleton and Vesicular Trafficking

This satellite meeting explored the latest advances in our understanding of neuronal polarity, in particular how cytoskeletal elements and trafficking fulfils these critical functions. Age-related defects in regulation and the dramatic consequences that lead to synapse elimination and/or neuronal degeneration was also discussed.

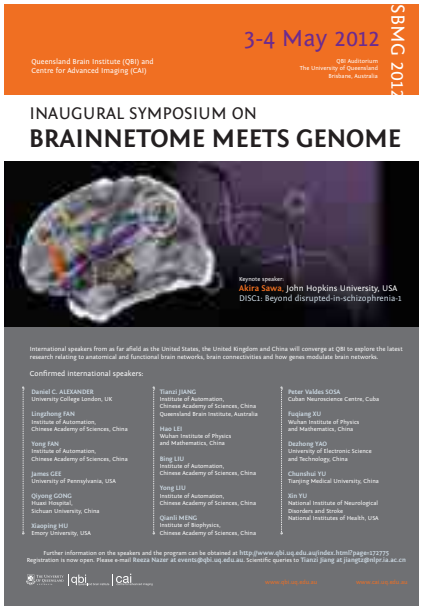
The meeting explored the critical role neuronal polarity plays in the development of the brain and how cytoskeleton and vesicular trafficking play both a structural and dynamic role in synaptic function.

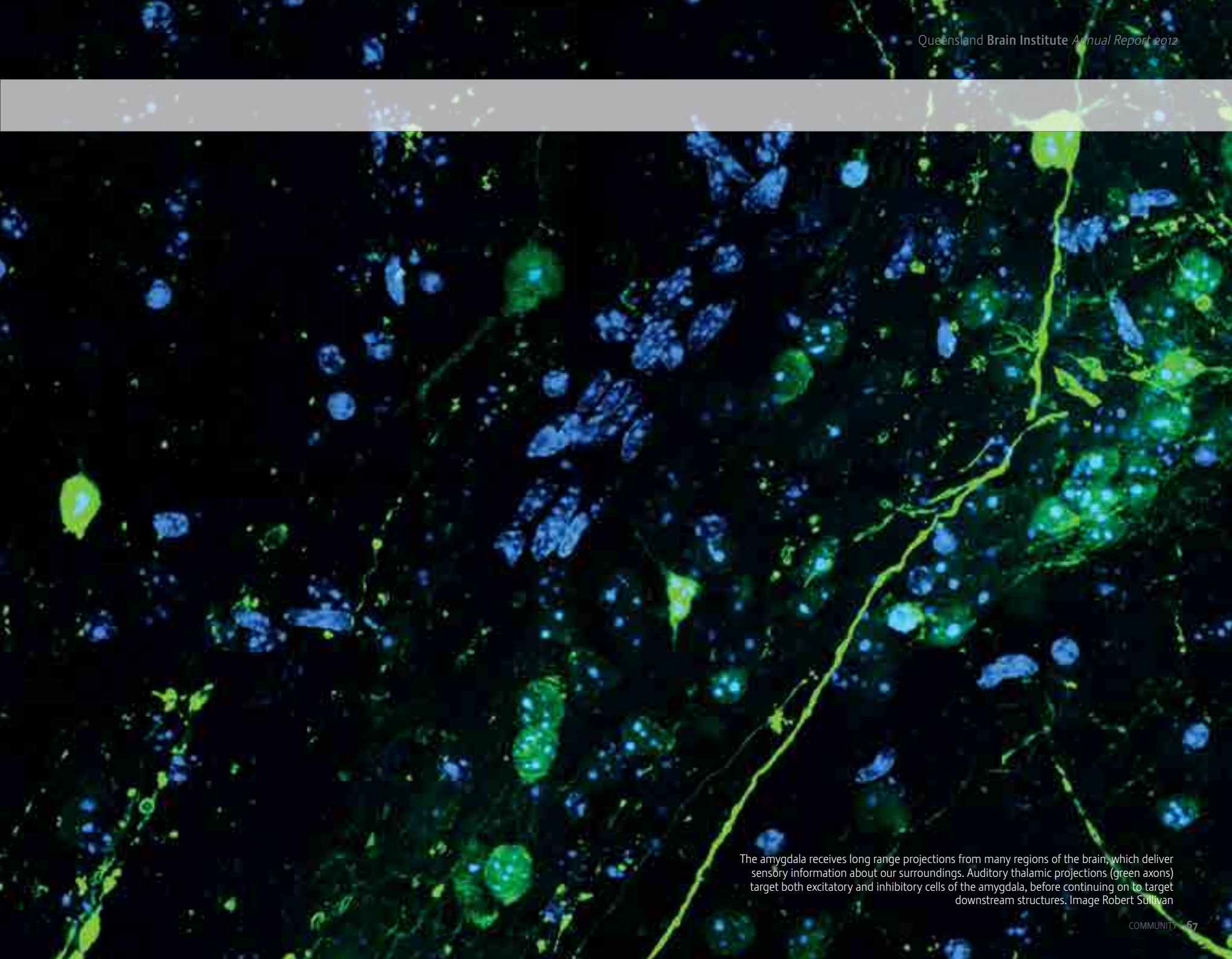
Lecture

Symposium on Brainnetome Meets Genome

QBI was host to the inaugural Symposium on Brainnetome Meets Genome (SBMG 2012) from May 3-4.

Keynote speakers included Dr Akira Sawa of The Johns Hopkins University, who discussed the Disrupted in Schizophrenia-1 (DISC1) gene in mice, and QBI's own Professor Geoffrey Goodhill, who explored computational models for the development of neural circuits.





The amygdala receives long range projections from many regions of the brain, which deliver sensory information about our surroundings. Auditory thalamic projections (green axons) target both excitatory and inhibitory cells of the amygdala, before continuing on to target downstream structures. Image Robert Sullivan

Merson Lecture

Brain Wiring and Disorders

QBI's annual Merson Lecture attracted one of the world's most respected neuroscientists, Professor Mriganka Sur, Newton Professor of Neuroscience and Director of the Simons Center for the Social Brain, Massachusetts Institute of Technology (MIT), Cambridge, USA.

In his address to a capacity crowd in QBI's auditorium, Professor Sur spoke of his extensive research into the human brain, "perhaps the most fantastic machine in the universe".

Professor Sur studies the organisation, development and plasticity of the cerebral cortex of the brain using experimental and theoretical approaches.

"It has billions of neurons, and each neuron interconnects with hundreds of other neurons via thousands of synapses – this staggering number of connections is one reason for the complexity of brain processing," he said.

"Networks are the engine of the brain, for they transform simple inputs to make complex outputs. "Understanding how the brain is wired is key to understanding how it works."

Research in Professor Sur's laboratory has demonstrated that specificity and plasticity are both fundamental requirements for brain wiring. The underlying mechanisms provide critical clues for repairing the brain after damage or disease.

He has discovered fundamental principles by which networks of the cerebral cortex are wired during development and change dynamically during learning.

The lecture is named in honour of Dr David Merson, member of the QBI Advisory Board, whose philanthropic sponsorship of this lecture is indicative of a growing community interest in neuroscience and the cutting-edge research that is being done in the area of neurological and mental diseases.

4th Brain Plasticity Symposium

Held at QBI in September, this symposium brought together leading national and international researchers in the field of neural mechanisms and plasticity to share their recent findings with the Australian neuroscience community.

The three-day event covered topics including learning and memory, circuits and cognition, circuits and plasticity, neurogenesis and cognition, ageing and cognition, and behavioural epigenetics, starting with a keynote lecture from Professor Jim McGaugh of the University of California, Irvine, USA on forming lasting memories.

The impressive line up of international speakers featured guests from USA, Canada, New Zealand, Japan and India.

2nd QBI-MCN Systems Neuroscience Symposium

The research collaboration between QBI and the Munich Center for Neurosciences (MCN) is progressing well.

A QBI delegation travelled to the Ludwig Maximilians University in Munich, home of the MCN, in October for the second Systems Neuroscience Symposium.

Here, the latest findings in sensory, cognitive, cellular and molecular neuroscience were showcased.

The event highlighted the local neuroscience community as a promising research environment for young scientists.

The symposium was unanimously regarded as a success.

Future collaboration concepts include a joint student PhD program, progressing research projects involving both long and short-term staff and student exchanges, as well as regular bilateral faculty visits.

Professor Jason Mattingley is now developing and planning the first subject-specific workshop to come out of the collaboration.

The workshop will focus on 'Cognitive Neuroscience and Imaging', and will be held at QBI in early 2014.

COMMUNITY OUTREACH

QBI's community outreach program is designed to engage people interested in discovering more about neurological disorders. The program's success is proof of the public's thirst to learn more about the latest developments in this area of research.

In addition to regular tours through QBI's world-class facilities, the Institute's researchers frequently conduct lectures, talks and discussions that are the anchor of the outreach program. This interaction – in libraries, bookstores, schools, hospitals and other community settings – has continually proven beneficial for the public and scientists alike.

As the community learns more about the world-leading research being conducted at QBI, the lectures provide an unparalleled opportunity for scientists to meet people who, in many cases, know someone affected by a neurological condition. Engaging with people who will potentially benefit from QBI's research in the longer term provides an additional impetus for the neuroscientists to advance their work.

In 2012, QBI's researchers were involved in more than 20 outreach events, including:

Associate Professor Elizabeth Coulson updated members of the Superannuated Commonwealth Officers' Association on the latest research into Alzheimer's disease.

Dr Francois Windels presented a talk to the Friends of Ipswich Library on addiction and the brain.

Dr Daniel Blackmore gave a presentation to members of the University of the 3rd Age, Petrie, about the effect of exercise on the brain.

Dr Luca Cocchi addressed the Bridgeman Downs Probus group at their monthly meeting, and spoke about brain dynamics underlying limits in human reasoning.

Associate Professor Bruno van Swinderen delivered a talk on using the genetic model *Drosophila melanogaster* to understand general anaesthesia and sleep to members of the Faculty of Pain (College of Anaesthetists).

Dr Michael Piper spoke to members of the Beenleigh Library about QBI's research into neurodegenerative diseases.

Associate Professor Naomi Wray spoke about her statistical research on mental health illnesses to staff and affiliates of Logan Adult Mental Health Services.

If your group would like to learn more about the exciting research at QBI and meet one of our researchers, contact QBI on 07 3346 6300.

Above: Members of Kenmore Village Probus Club visited QBI in November.
Right: 2012 Gala Art Exhibition fundraiser held by Soroptimist International Brisbane South (SIBS). From Left, Dr Robyn Wallace, QBI; Jan Skinner, President, SIBS; Penelope Gilbert Ng, President, Pastel Society of Australia.

AUSTRALIAN BRAIN BEE CHALLENGE

out-smart, out-think, out-last

The Australian Brain Bee Challenge (ABBC) has been encouraging high school students to learn about neuroscience since 2006. The program is designed to capture students' interest in brain structure, function and anatomy, and to educate students, teachers and the wider community about the importance of neuroscience research to society. The ABBC provides opportunities for students from all over Australia, including regional areas, to participate and consider a career in science and in particular, neuroscience.

2012 was a fantastic year for the ABBC, with Brisbane State High School student and 2011 ABBC Champion, Teresa Tang, becoming the first Australian student to win the International Brain Bee Championship, held in Cape Town, South Africa in July 2012. Teresa competed against students from 14 different countries and completed five neuroscience challenges that tested her knowledge of neuroscience topics including neuroanatomy, neurohistology and disorders of the nervous system, to become the International winner.

The ABBC has three rounds, with Round 1 taking place during the annual Brain Awareness Week in March. Round 1 of the ABBC is an online quiz in which Year 10 students have to demonstrate their knowledge and understanding of brain structure, function, anatomy, neurological disease and disorders. In 2012, there were 5,331 Year 10 student participants in Round 1, taking the total number of participants to 23,878 over the 7 years since the ABBC was introduced in Australia.

The Round 2 Queensland event took place at the Queensland Brain Institute (QBI) on 19 June 2012, with Nobel Laureate Professor Elizabeth Blackburn addressing 200 students and teachers. The Year 10 students came from all over Queensland, including Cairns, Rockhampton and Townsville. In addition to participating in the competition, students and teachers had the opportunity to tour the facilities at QBI, observe experiments and hear from QBI scientists discussing their research, discoveries and how they became involved in science research as a career.

Round 3, the National Final, in which each State Champion competes to become the Australian Brain Bee Champion, is held annually at the Australian Neuroscience Society meeting. The Australian Brain Bee Champion for 2012 will be decided at the ANS meeting in February 2013 in Melbourne. The winner will attend the International Brain Bee Competition in Vienna, Austria in September 2013.

In 2012, the ABBC and QBI also collaborated with the Queensland Aboriginal and Torres Strait Islander Foundation (QATSIF) to give three Indigenous students from Far North Queensland the opportunity to spend a week at QBI experiencing what it is like to be a neuroscientist.

With neurological and mental illness accounting for almost half of the total disease burden in Australia, the ABBC is one way students can be encouraged to be more interested in neuroscience research and to join the researchers at QBI in finding treatments and cures for disease. The ABBC is continuing to develop meaningful ways to engage students, teachers and the community and hopes the ABBC will continue to get bigger and better in 2013.

Right: Teresa Tang, the 2011 Australian and International Brain Bee Champion from Brisbane State High School.

RECOGNITION

Microscopy Services Manager Luke Hammond.

Recognition

The Queensland Brain Institute is home to nearly 300 dedicated researchers working to discover the cellular and molecular mechanisms that underlie the ability of the adult brain to generate new nerve cells and form functional connections. QBI researchers consistently shine in the neuroscience community, representing the Institute on a number of pivotal scientific organisations and serving on prestigious editorial boards.

QBI's track record in terms of publications, grants and awards further attests to the high standard of research being undertaken with the aim of discovering the fundamental mechanisms regulating brain function.

FELLOWSHIPS AND AWARDS

Australian Research Council

Discovery Outstanding Researcher Award

As part of Australia's largest individual ARC Discovery Project grant to commence in 2012, Professor Justin Marshall received a prestigious Discovery Outstanding Researcher Award, making him one of only 26 recipients Australia-wide. During the course of his three-year study Professor Marshall will investigate the neural processing that underpins the sophisticated forms of colour and polarisation vision exhibited by cephalopods (octopus and squid) and crustaceans (mantis shrimps) on the Great Barrier Reef, and will determine how these sensory strategies facilitate the communication and survival of these species.

Future Fellowship

Dr Michael Piper, a joint appointment between the School of Biomedical Sciences and QBI, has taken the next step in an already impressive research career with the awarding of a Future Fellowship. Designed to support the most talented researchers with the potential to boost Australia's research and innovation capacity, this fellowship will fund Dr Piper to investigate the transcriptional control of neural stem cell differentiation.

Uncovering the genetic and molecular mechanisms that modulate this differentiation will have critical implications for our understanding of both normal development and disease processes, and may also provide essential knowledge that will facilitate the future development of therapeutic treatments for neurodegenerative conditions and brain cancer.

Discovery Early Career Researcher Award

In the first round of the ARC's new Discovery Early Career Researcher Award scheme, which has been implemented to identify research excellence and leadership potential in young investigators at the beginning of their careers, Dr Oliver Baumann has excelled. In a pool of over 2100 applicants, of whom only 13 per cent were successful, this is a considerable achievement. Dr Baumann will use neuroimaging techniques to probe the role of the human cerebellum in perceptual processes. Traditionally considered as a regulator of motor function, it has only recently become apparent that the cerebellum is also implicated in a number of neurological conditions that are also characterised by perceptual and cognitive deficits, including autism, schizophrenia and attention deficit hyperactivity disorder. A more complete understanding of the structure and function of the cerebellum therefore has the potential to inform better diagnosis and treatment of such conditions.

National Health and Medical Research Council

Early Career Fellowship

Dr Peter Kozulin was the recipient of a CJ Martin Overseas Biomedical Fellowship, the goal of which is to study the neurodevelopment of the visual system by focussing on hindbrain development, and the visual and neurological consequences that result from malformation of this structure. During the first two years of his fellowship, Dr Kozulin will work with Dr Alain Chédotal at the Institut de la Vision in Paris, before returning to Australia to spend the next two years in the laboratory of QBI's Professor Linda Richards. Dr Kozulin's long-term objective is to establish an independent group investigating the application of molecular therapies for the treatment of visual and neurodevelopmental disorders.

Human Frontier Science Program

HFSP Long-term Fellowship

Dr Rosina Giordano-Santini was recently awarded a Human Frontier Science Program Long-term Fellowship, for research to be conducted in the laboratory of QBI's Dr Massimo Hilliard. Here Dr Giordano-Santini will study the molecular mechanisms regulating the establishment and maintenance of neuronal integrity. The neuron theory of one of the fathers of neuroscience, Ramón y Cajal, states that the relationship between nerve cells is not one of continuity but rather of contiguity. Although demonstrated in every species investigated, our understanding of the processes that maintain neuronal individuality is still based only on morphological observations. Dr Giordano-Santini will focus on defining the molecular elements that generate and regulate this critical aspect of nervous system structure and function.

Awards

Member of the Order of Australia

In recognition of his highly distinguished career, 2012 saw Professor Mandyam Srinivasan appointed a Member of the Order of Australia (AM) for outstanding achievement and service. Professor Srinivasan, a Fellow of the Royal Society of London as well as the Australian Academy of Science, received his award "for service to visual and sensory neuroscience through the Queensland Brain Institute, as an academic, researcher and mentor, and to the national and international scientific community". This follows the 2006 Prime Minister's Prize for Science and the UK Rank Prize in Optoelectronics in 2008, a truly stellar achievement.

Australasian Society for Psychiatric Research Founders' Medal

Professor John McGrath was also honoured in 2012 as the recipient of the Australasian Society for Psychiatric Research (ASPR) Founders' Medal, awarded annually to a person who, over their course of career, has made a significant contribution to psychiatric research. This recognition is testament to the esteem in which Professor McGrath is held by his peers and to his outstanding commitment to and achievements in psychiatric research, in particular his work to generate and evaluate non-genetic risk factors for schizophrenia.

The University of Queensland Foundation Research Excellence Awards

In 2012, Dr Oliver Baumann was one of only eight researchers to be honoured with a UQ Foundation Research Excellence Award, designed to recognise early to mid career research excellence and leadership potential. Dr Baumann will use his funding support to investigate the role played by the human cerebellum in the regulation of emotion. This work will provide a better understanding of, and potential treatment for, a range of disorders that have been linked to cerebellar dysfunction, including schizophrenia, autism and depression.

COMMERCIALISATION

During 2012, QBI continued to develop promising new molecules and methods for treatment of neurodegenerative diseases, neuropsychiatric disorders, stroke and acute spinal cord injury.

A groundbreaking international initiative has brought together eminent researchers from QBI, the Shanghai Changzheng Hospital, UQ Diamantina Institute and the Centre for Advanced Imaging at UQ. Financially supported by NuNerve Pty Ltd, UQ, the Shanghai Changzheng Hospital and the ARC Linkage program, the researchers (Professor Matthew Brown, Professor Perry Bartlett, Professor Huji Xu, Professor Peter Visscher, Professor David Reutens, Professor Bryan Mowry and Dr Robyn Wallace) will undertake large population studies to identify genes that are associated with motor neuron disease, schizophrenia and stroke. The project will determine genetic markers, aid development of diagnostic tools and identify new therapeutic targets for these debilitating neurological disorders.

Software tools were developed in the areas of cell sorting (Mr Geoffrey Osborne) as well as prediction of risk associated with developing neuropsychiatric disorders (Associate Professor Charles Claudianos). In addition, two provisional patent applications were filed around methods of treatment of anxiety disorders, further funding was secured to continue a collaborative research project with a global aviation company (Professor Mandyam Srinivasan) and a new target for treating ischaemic stroke was discovered (Associate Professor Frederic Meunier).

With support from the ARC Linkage program and NuNerve Pty Ltd, QBI researchers began a three-year project that is focussed on developing and validating a new treatment for neurodegenerative disorders, including motor neuron disease (Professor Joe Lynch and Professor Pankaj Sah). The treatment involves silencing excessive neuronal activity using a safe, commonly prescribed drug.

QBI researchers continued to develop an active molecule that promotes nerve survival and prevents motor neuron loss (Associate Professor Elizabeth Coulson and Dr Timothy Bredy). A therapy developed from this research can be targeted towards treating the neuronal cell death that causes the neurodegenerative condition rather than simply modulating the side-effects or minimising the symptoms. QBI has partnered with NuNerve Pty Ltd to conduct an ARC Linkage project, which entered its second year during 2012.

QBI's commercialisation activities are supported by UniQuest Pty Ltd, the main commercialisation company of UQ. UniQuest provides commercialisation expertise and resources through a Manager of Innovation and Commercial Development, Dr Bronwyn Battersby, who is based at QBI.

Left: Associate Professor Elizabeth Coulson.

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GRANTS

The following contains information on national and international competitive funding for both fellowships and research grants that received funding starting in 2012; GST and other yearly increments are not included in the amounts shown. Internal grants or fellowships awarded by The University of Queensland are not included here.

Australian Government, Department of Industry, Innovation, Climate Change, Science, Research and Tertiary Education

Australia Awards 2012 - Endeavour Executive Award

Zifarelli G – Endeavour Executive Award, $18,500, 1 year

Inspiring Australia – National Science Week Grants

Dean A (CoralWatch) - Corals at your Doorstep - educating youth in South East Queensland about corals in Moreton Bay, $10,780, 1 year

Australian Research Council

Future Fellowship

Piper M - Transcriptional control of neural stem cell differentiation during development and disease, $684,422, 4 years [awarded to and administered by UQ School of Biomedical Sciences, Piper has a 50% SBMS, 50% QBI appointment]

Discovery Early Career Researcher Award

Baumann O - The role of the human cerebellum in perceptual processes, $375,000, 3 years

Discovery Projects

Claudianos C, Reinhard J - Role of micro-RNAs in learning and memory of insects, $285,000, 3 years

Lynch J, Keramidas A - Understanding the mechanisms of GABA type-A receptor activation and drug modulation, $285,000, 3 years

Marshall J - New dimensions in colour and polarisation vision on The Great Barrier Reef, $962,000 including Distinguished Outstanding Researcher Award, 3 years

Meunier F - The role of actin in driving bulk endocytosis in neurons and neurosecretory cells, $378,000, 3 years

Reinhard J, Claudianos C - Plasticity in the periphery: how sensory experience modulates the sense of smell, $310,000, 3 years

Remington R, **Mattingley J**, Becker S, F - Cortical regulation of attentional capture $334,000, 3 years [awarded to and administered by UQ School of Psychology]

Visser T, Enns J, **Cunnington R** - Why being lost-in-thought can blind you: the effects of distractor processing on perception, $223,590, 3 years [awarded to UQ School of Psychology and currently administered by University of Western Australia].

Linkage Project

Lynch J, Sah P - New tools to activate and silence neural circuits, $458,933, 3 years

Autism Queensland Inc.

Claudianos C - Validating the potential for a 'Genome Analysis Tool' for autism spectrum disorders, $110,000, 1 year

Boeing Defence Australia

Srinivasan M - Assessment and development of bio-inspired guidance navigation and control (GNC) sensors, algorithms and solutions for unmanned aircraft systems, $65,000, 1 year

European Molecular Biology Organization

Long-term Fellowship

Matamelas M - Selective vulnerability in Alzheimer's disease and related disorders: Mechanism of tau pathology, ~$140,000, 2 years [awarded 2009, transferred to QBI in 2012]

Short-term Fellowship

Osborne S - Role of PIKfyve in pre- and post-synaptic membrane trafficking in the central nervous system, $11,397 1 year

Human Frontier Science Program

Human Frontier Science Program Long-term Fellowship

Giordano-Santini R - Neuronal identity and control of neurite fusion during development, $225,900, 3 years

Marie Curie Actions European Commission

International Outgoing Fellowships

Dupierrix E - Dynamic and plasticity of spatial perception and attention neural processes, 4 years [awarded to and administered by CNRS]

Motor Neurone Disease Research Institute of Australia Inc.

Grant-in-Aid

Wallace R, Hilliard M - Analysis of TDP-43 target genes in *C. elegans*, $93,000, 1 year

National Health and Medical Research Council

Training (Postdoctoral) Fellowship

Anggono V - NHMRC Training Fellowship (CJ Martin Overseas-based Biomedical): The role of stargazin and TARP phosphorylation in synaptic plasticity, 4 years [awarded to Children's Medical Research Institute, Sydney, 2008, transferred to QBI in 2012]

Benyamin B - NHMRC Training Fellowship (Australian-based Biomedical): Genome-wide association studies of biomedical traits and endophenotypes for complex disease, $285,000, 4 years [awarded to QIMR, 2009, transferred to QBI in 2012]

Kozulin P - NHMRC Training Fellowship (CJ Martin Overseas-based Biomedical): Controlling the development and function of hindbrain commissures in vertebrate animals: the role of Robo3 receptor, $336,852, 4 years

Project Grants

Götz J, Ittner, L - Selective vulnerability in Alzheimer's disease and related disorders: mechanism of tau pathology, $1,026,728, 4 years [awarded 2011, transferred to QBI in 2012]

Bredy T - Exploring DNA methylation as a mechanism for long-term memory for fear extinction, $401,250, 3 years

Collins B, Teasdale, R, **Coulson, E,** King, G – Endosomal protein sorting and APP processing in Alzheimer's disease, $180,625, 1 year [awarded to and administered by UQ Institute for Molecular Bioscience]

Cooper H - Neogenin: a molecular determinant of neural progenitor polarity and function, $549,366, 3 years

Eyles D, Burne T, McGrath J - Developmental vitamin D deficiency and prefrontal cortical dysfunction, $343,510, 3 years

Mattingley J, Dux P, Molenberghs P - Efficacy of prism adaptation for recovery of brain function in unilateral spatial neglect, $513,675, 3 years

Mattingley J, Riek S, Carroll T, **Kamke M**, **Sale M** - The role of attention in modifying neural plasticity in the adult human cortex, $378,510, 3 years

Piper M, **Richard L,** Boyd A, Bailey T - Nfib regulates glial differentiation during development and disease via repression of the key epigenetic protein, Ezh2, $553,675, 3 years

Richards L - Molecular and activity-dependent mechanisms regulating the targeting of corpus callosum axons in the contralateral hemisphere, $399,263, 3 years

Program Grant

Halliday G, **Götz J,** Ittner L, Kril J, Hodges J, Kiernan M - Frontotemporal dementia and motor neurodegenerative syndromes, $11,011,390, 5 years [awarded to and administered by the University of New South Wales]

GRANTS

Organization for Human Brain Mapping

Li Y - Trainee Abstract Award for the 2012 OHBM Annual Meeting in Beijing, China, $700, 1 year

Queensland State Government

Queensland International Fellowship Travel Award

Meunier F - Deciphering the puzzle of molecular events underpinning neurotransmission using super-resolution microscopy, $21,000, 1 year

PhD Top-up Scholarship

Turner K – Smart Futures PhD top-up scholarship, $12,000, 3 years

Queensland-Smithsonian Fellowship Program

How M - Polarisation vision in fiddler crabs, $17,000, 1 year

UniQuest

Pathfinders

Osborne G – Slice and dice sorting software, $15,000, 1 year.

US Department of the Air Forces

Asian Office of Aerospace Research and Development

Marshall J - Re-engineering the stomatopod eye, nature's most comprehensive visual sensor, $284,793, 1 year

Above: Associate Professor Ross Cunnington observing a participant in the MRI scanner.

NEUROSCIENCE SEMINARS

The Queensland Brain Institute conducts a weekly seminar program giving neuroscientists an opportunity to learn more about the latest scientific developments, often before research is published. The series is designed to challenge researchers in their thinking, promote excellence through the exchange of ideas and lead to future collaborations.

Professor Kirill Alexandrov
Institute for Molecular Bioscience,
The University of Queensland
Three cornerstones of protein research: platform technologies, enabling tools and new discoveries

Mr Daniel Avesar
Dartmouth College, Hanover, USA
Selective serotonergic modulation of cortical pyramidal neurons

Professor James Bamburg
Department of Biochemistry and Molecular Biology,
Colorado State University, Fort Collins, USA
ADF/cofilin in neuronal development and disease

Associate Professor John Bekkers
Eccles Institute of Neuroscience,
Australian National University
Cortical sensory processing and epilepsy: insights from the olfactory system

Dr Gilyana Borlikova
Queensland Brain Institute, The University of Queensland
Why bother with behaviour? And what can you do here at QBI if you decide to proceed

Associate Professor James Bourne
Faculty of Medicine, Nursing and Health Sciences, Monash University
The adaptive visual brain: lessons from development and lesions

Dr Holly Bridge
Department of Clinical Neurology, Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, University of Oxford, UK
Investigating the 'visual system' in the absence of light input

Associate Professor Deborah Brown
School of History, Philosophy, Religion and Classics, The University of Queensland
Free will, attention and other olde good things

Professor Alon Chen
Department of Neurobiology, Weizmann Institute of Science, Israel
Dissecting the central stress response using site-specific genetic manipulation in adult mice

Professor Stephanie Clarke
Medicine Department, Service of Neuropsychology and Neurorehabilitation, Université de Lausanne, Switzerland
Roaring lions and chirruping lemurs: how the brain codes sound objects in space

Associate Professor Helen Cooper
Queensland Brain Institute, The University of Queensland
Neogenin controls neural stem cell structure and function

Associate Professor Elizabeth Coulson
Queensland Brain Institute, The University of Queensland
A central role for cholinergic dysfunction in cognitive decline and neurodegeneration in Alzheimer's disease

Associate Professor Ross Cunnington
Queensland Brain Institute and School of Psychology, The University of Queensland
Brain processes underlying the planning and perception of actions

Professor Barry Dickson
The Research Institute of Molecular Pathology, Austria
Wired for sex: the neurobiology of Drosophila *courtship behaviour*

Professor Valsa Eapen
School of Psychiatry, University of New South Wales
Tourette Syndrome: tracing the developmental trajectory from genes to behaviour

Professor Francois Feron
Université Aix Marseille, France
Human nasal olfactory stem cells: a new subtype of mesenchymal stem cells and a promising tool for understanding and repairing the brain

Associate Professor Cecilia Flores
Department of Psychiatry, McGill University, Canada
Netrin-1 receptors organize dopamine circuitry and may contribute to differential vulnerability to psychopathology

Ms Clare Giacomantonio
Queensland Brain Institute, The University of Queensland
Creating the cortex: mechanisms of cortical development

Ms Ilan Gobius
Queensland Brain Institute, The University of Queensland
The role of commissural plate glia, Slit and FGF protein family members in forebrain commissure formation

Professor Geoffrey Goodhill
Queensland Brain Institute and School of Mathematics and Physics, The University of Queensland
Computational models of neural wiring development

Dr Brett Graham
School of Biomedical Sciences and Pharmacy,
University of Newcastle, NSW
Pleasure and pain: studies from the lateral hypothalamus to the spinal dorsal horn

Mr Luke Hammond
Queensland Brain Institute, The University of Queensland
Microscopy in the age of complexity

Dr Martin How
Queensland Brain Institute, The University of Queensland
Whole-field polarisation vision in crustaceans

Dr Christine Jasoni
Department of Anatomy, University of Otago, New Zealand
You are what ~~you~~ your mother eats: effects of maternal diet on fetal hypothalamic circuitry development

Professor Graham Kerr
School of Exercise and Nutrition Sciences,
Queensland University of Technology
Freezing and shaking: understanding postural instability and gait disability in Parkinson's disease

Professor Simon Laughlin
Cambridge Neuroscience, University of Cambridge, UK
What makes brains energy efficient?

Professor Joe Lynch
Queensland Brain Institute, The University of Queensland
Developing drugs for chronic inflammatory pain

Ms Han Lu
Queensland Brain Institute, The University of Queensland
Investigating glycine receptor function and structure using voltage-clamp fluorometry

Professor John McGrath
Queensland Brain Institute and Department of Psychiatry, The University of Queensland
The 'selfish sperm', advanced paternal age and adverse brain outcomes – an update on new data and new hypotheses

Dr Sara Mednick
Department of Psychiatry, University of California, San Diego, USA
What can sleep stages tell us about the mechanisms of memory consolidation?

Professor Grant Morahan
Western Australian Institute for Medical Research
Powerful new resources for discovery of genes for complex traits

NEUROSCIENCE SEMINARS

Dr Rebecca Nisbet
Division of Materials Science and Engineering, CSIRO, Melbourne
Controlling the uncontrollable: using scaffold proteins to stabilise the amyloid-ß peptide

Professor Anna Christina (Kia) Nobre
Cognitive Neuroscience, University of Oxford, UK
Pre-membering perception

Professor Hideyuki Okano
Department of Physiology, Keio University, School of Medicine, Japan
The iPS and direct reprogramming technologies for investigating CNS disorders and regeneration

Dr Alessandra Pierani
Development Neurobiology, Institut Jacques Monod, Université Paris, France
Migrating transient signaling neurons and patterning of the cerebral cortex

Dr Megan Porter
Department of Biological Sciences, University of Maryland, Baltimore County, USA
Molecular evolution of vision in mantis shrimp: a multifaceted approach

Assistant Professor Nicholas Priebe
School of Biological Sciences, University of Texas at Austin, USA
Disrupting ocular integration in primary visual cortex

Professor Linda Richards
Queensland Brain Institute, The University of Queensland
Wiring the brain for function: how axons of the corpus callosum find their targets in the contralateral hemisphere

Professor Gunter Schumann
MRC-SGDP Centre, Institute of Psychiatry, King's College, London, UK
Neurobehavioural analysis of reinforcement and its relevance for alcohol abuse: results from the IMAGEN study

Dr Surya Singh
School of Information Technology and Electrical Engineering, The University of Queensland
Moving naturally: agile motion analysis and generation

Professor Mandyam Srinivasan
Queensland Brain Institute and School of Information Technology and Electrical Engineering, The University of Queensland
Collision avoidance, target pursuit and motion camouflage in flying honeybees

Mr Gavin Taylor
Queensland Brain Institute, The University of Queensland
Combining visual and air flow cues for honeybee flight control

Professor Gregor Thut
Department of Psychology, University of Glasgow, UK
Interacting with human brain oscillations by rhythmic TMS to change attention and perception

Associate Professor Naotsugu Tsuchiya
Laboratory for the Neuronal Basis of Consciousness, School of Psychology and Psychiatry, Monash University
Visual consciousness tracked with direct intracranial recording from low- and high-level visual cortices in humans and monkeys

Dr Madhusudhan Vekadesan
National Centre for Biological Sciences, Tata Institute of Fundamental Research, Bangalore, India
How to throw at high speeds, accurately, and accurately at high speeds

Professor Patrik Verstreken
Neuronal Communication Laboratory, VIB Center for the Biology of Disease, Belgium
Mitochondrial and synaptic dysfunction in Parkinson's disease

Dr Robyn Wallace
Queensland Brain Institute, The University of Queensland
Characterisation of RNA bound to TDP-43, a protein involved in neurodegenerative diseases

Assistant Professor Jack Waters
Department of Physiology, Northwestern University, Chicago, USA
Activation of nicotinic receptors on deep-layer neocortical pyramidal neurons by synaptically-released ACh

Associate Professor Stephen Williams
Queensland Brain Institute, The University of Queensland
Behaviourally relevant dendritic integration in retinal and neocortical circuits

Professor Ding Xue
Molecular, Cellular and Development Biology, University of Colorado, Boulder, USA
Programmed cell death and lipid asymmetry

Mr Jiajia Yuan
Queensland Brain Institute, The University of Queensland
Mechanisms of axon guidance by molecular gradients

Professor Murat Yucel
Centre for Youth Mental Health, Melbourne Neuropsychiatry, The University of Melbourne
The impact of cannabis use on cognitive functioning and brain structure: implications for understanding the neural basis of psychosis

Dr Qiongyi Zhao
Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, China
Genomic and transcriptomic applications based on NextGen Sequencing

Above: Lecture attendees in the QBI Auditorium.

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In addition to playing a role in grant assessment for major national and international funding bodies, our staff provide the following external professional service to the discipline.

Perry Bartlett
- Australian Academy of Science, Animal Sciences Committee Member
- Centre for Brain Research, University of Auckland, Scientific Advisory Board Member
- Garvan Institute of Medical Research, University of New South Wales, Scientific Appointments and Promotions Committee Member
- Motor Neurone Disease Research Institute of Australia, Research Committee Member
- NHMRC Assigners Academy Member
- Queensland Chapter of the Australian Academy of Science, Chair

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- Australian Neuroscience Society Scientific Program, Advisory Group Member
- Australian Huntington's Disease Association, Queensland Branch, QBI representative
- Australian Neuroscience Society Scientific Annual Meeting, Member of the Local Organising Committee

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- Australian Brain Bee Challenge, Northern Territory Coordinator
- Australian Neuroscience Society, National Council Member
- Friedreich's Ataxia Research Association, Scientific Advisory Committee Member
- NHMRC Grant Review Panel Member
- Joint NHMRC-Alzheimer's Australia Dementia Care Knowledge Translation Consultation Group, Panel Member

Ross Cunnington
- Australasian Cognitive Neuroscience Society, National President

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- Neural Information Processing Systems Conference, Program Committee, Area Chair

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- Member of the Alzheimer Research Forum
- Member of the DZNE (German Center for Neurodegenerative Diseases) Scientific Review Panel

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- Medical Image Computing and Computer Assisted Intervention Society, Member of Board of Directors

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- National Collaborative Research Infrastructure Strategy Imaging Facilities, Board Member

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- Program Committee Member, International Society for Developmental Neurobiology meeting, Mumbai
- Scientific Advisor to Australian Disorders of the Corpus Callosum (AusDoCC)

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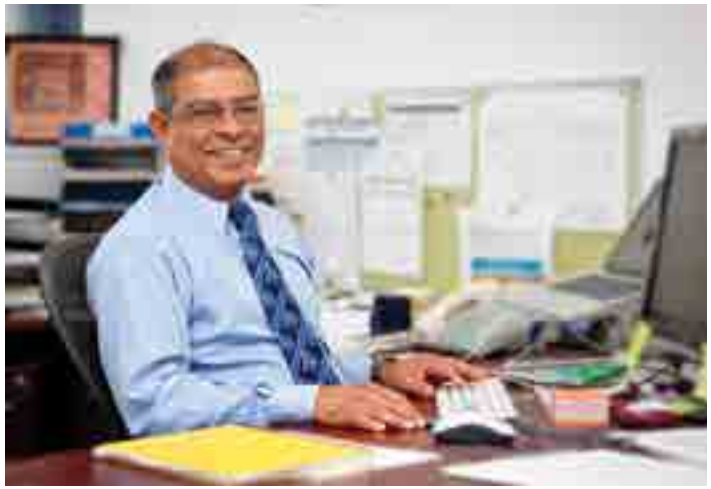

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Dr Daniel Gilbert
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Dr Zhe Yang
Dr Qiongyi Zhao (began June)
Dr Yanqiong Zhou (began July)

Research Officers
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Ilan Gobius (began July finished October)
Sepideh Keshavarzi (began April)
Richard Moore (began July finished August)
Yangiong Zhou (began April finished July)

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Anne-Sophie Bedin
Clement Bonini (finished February)
Zoran Boskovic (finished January)
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Shanzhi Yan (began July)
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Joon Yong An (began April)
Samuel Baker
Sian Louise Baker (began October)
Danay Baker-Andresen
Jessica Barnes
Stephanie Biergans (began April)
Anna Bode
Zoran Boskovic (began May)
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Gerhard Leinenga (began April)
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Cirong Liu (began October)
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Sha Liu
Roger Marek
Andrew Martin
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Above: Irek Porebski is part of QBI's IT team.

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