qbi

THE FIRST 1000 DAYS

2003 – 2006

The University Of Queensland
AUSTRALIA

qbi queensland brain institute

MESSAGE FROM THE **VICE-CHANCELLOR**

I am delighted *with the progress and achievements of The University of Queensland's world-class neuroscience research facility, the Queensland Brain Institute (QBI).*

On both a personal and professional level, it gives me enormous pleasure to see QBI forging a strong reputation in the internationally competitive field of neuroscience.

QBI's growth and success are founded on scientific excellence, and the generous support of The Atlantic Philanthropies and the Queensland Government. Working with UQ, their generosity has enabled construction of a $63 million purpose-built neuroscience research facility and the subsequent purchase of state-of-the-art technology to equip the building.

This document, "QBI – The First 1000 Days", showcases the Institute's first three years, highlighting its research themes, staff and discoveries.

QBI's primary objective is to discover the fundamental mechanisms regulating brain function, particularly those controlling the formation of new nerve connections and the generation of new nerve cells.

Better understanding of these fundamental mechanisms is essential to the development of therapeutic treatments for neurological conditions such as dementia, stroke, motor neuron disease, brain and spinal cord injury, and depression.

QBI continues to attract high calibre neuroscientists, adding to a community of some 1000 scientists and engineers currently working at UQ's four Smart State research institutes.

QBI's inaugural Director, Professor Perry Bartlett, is a Federation Fellow and holds the Foundation Chair in Molecular Neuroscience at UQ. He has built an Institute that is set to expand its scientific influence throughout the Asia–Pacific region.

I congratulate Professor Bartlett for the energy and leadership he has brought to Queensland, building on a long history of neuroscience research at UQ.

Centres such as QBI are investments in the future health and wellbeing of people throughout Australia and the world. These centres represent an ideal combination of the Queensland Government's Smart State funding, the generosity of The Atlantic Philanthropies and UQ expertise.

Professor John Hay AC
Vice-Chancellor
The University of Queensland

THE QUEENSLAND BRAIN INSTITUTE

SECTION ONE

1

Research under way at QBI is vital to the development of treatments for dementia, stroke, motor neuron disease, brain/spinal cord injury and depression.

<<<< qbi — the first 1000 days

THE QUEENSLAND BRAIN INSTITUTE

THE QUEENSLAND BRAIN INSTITUTE

FROM **THE DIRECTOR**

QBI's continued growth as a world-leading neuroscience institute is all but assured.

The establishment of the Queensland Brain Institute (QBI) in late October 2003 was the result of an amazing confluence of ideas and foresight by three great community leaders, The University of Queensland's Vice-Chancellor, John Hay, the founder of Atlantic Philanthropies, Chuck Feeney, and the Premier of Queensland, Peter Beattie. They provided the impetus and the resources for a $63 million state-of-the-art building to be completed in late 2007, and gave me the unprecedented opportunity to recruit a faculty of world-class neuroscientists.

It all began a year earlier, in 2002, when I relocated my group from the Walter and Eliza Hall Institute in Melbourne, where I was head of the Division of Neurobiology and Development, to lay the foundations for a new Institute as the inaugural Chair in Molecular Neuroscience. Although the funding for such an Institute was uncertain at the time, the Vice-Chancellor's clear and steadfast vision that neuroscience was an area of research in which UQ should excel and become an international leader was compelling. He quickly engaged the Atlantic Philanthropies and the Queensland Government in this concept, as a result of which QBI was born. Today, QBI takes its place alongside the Australian Institute of Bioengineering and Nanotechnology (AIBN) and the Institute for Molecular Bioscience (IMB), as part of the revolution that has occurred in the biosciences at The University of Queensland under the leadership of the Vice-Chancellor.

QBI was established with the specific aim of discovering the fundamental mechanisms that control higher brain functions, such as learning and memory, as this is the last scientific frontier to be conquered if we are

to fully understand human behaviour and that allusive human characteristic of consciousness or self awareness. Moreover, I believe that such an understanding will lead to revolutionary new therapeutics to combat the neurological and mental illnesses that ever-increasingly affect both our young and aged population.

As a step towards achieving these goals, I am delighted to report that, since its establishment, QBI has attracted some of the best neuroscientists from within Australia and from overseas. Professor Pankaj Sah joined the Institute shortly before its formal inception and has been enormously important in its growth and success over the first 1000 days. In recognition of his pivotal role and his outstanding scientific leadership,

he has recently been appointed as the Deputy Director for Research. We have also enticed exceptional young scientists such as Associate Professor Linda Richards and Dr Robyn Wallace back to Australia from the USA, as well as attracting several distinguished international scientists such as Professor Brent Reynolds and Associate Professor Geoffrey Goodhill. Since arriving at QBI, these faculty members have established new groups and have proven highly successful in attracting both Australian and international funding.

I was especially delighted to have Professor Reynolds join us, as together with Associate Professor Richards and myself in Australia, his group in Canada independently reported in 1992 that there are stem cells in the brain capable of giving rise to new neurons. This has since become one of the hottest areas in neuroscience and it is wonderful to have the originators of this field working together at QBI.

More recently, we have been joined by the recipient of the 2006 Prime Minister's Prize for Science, Professor Mandyam Srinivasan, who heads QBI's visual and sensory neuroscience research team, and Professor Jason Mattingley, who will head QBI's new cognitive neuroscience team. Our next annual report will no doubt include a more comprehensive update on the work of these two leading scientists. Although working in widely different animal models and using a range of different techniques, all these scientific groups focus on understanding important mechanisms that regulate the development of a functional brain.

QBI's research primarily focuses on the mechanisms that regulate brain plasticity – the ability of the brain to change neuronal connections and even its nerve cell complement. This is because we increasingly believe that this is the very basis of how functions such as learning and memory are regulated, and how information is stored. Thus, understanding the regulation of these processes offers the promise not only of promoting life-long cognitive health, even in the older population, but also, because of the plastic nature of the system, of developing a new generation of therapeutics to treat the avalanche of neurological and mental ill-health that accounts for almost half of the disease burden of our community. As you will see within the pages of this report, the Institute's research is strategically targeted to help understand the key aspects regulating brain plasticity and how this information can be applied to alleviating the dreadful consequence of brain disease in our community.

I am pleased to report that QBI scientists and their collaborators have made significant advances in several key areas, leading to publication in frontline journals such *Nature Neuroscience* and *Journal of Neuroscience*. These include identifying a molecule that blocks the regrowth of damaged nerve processes, a protein that dramatically inhibits brain cancer stem cells in laboratory animals, and a molecule that plays a key role in establishing the major nerve connections between each side of the brain, as well as defining a mechanism for how neurogenesis is regulated in the brain.

However these achievements have not occurred in a vacuum. QBI's weekly neuroscience seminars are an essential element in our continuing success, and have become an intra-campus focus for exploration and development of ideas. These seminars

THE QUEENSLAND BRAIN INSTITUTE

During the past three years, more than 100 scientists have participated in this lecture series

are often the catalyst for the inspired thinking which leads to valuable new approaches at the laboratory bench.

During the past three years, more than 100 scientists have participated in this lecture series. This important facet of scientific discourse at QBI will no doubt benefit from our imminent move into larger facilities. While it is important that we exchange ideas with our scientific colleagues in Australia, it is equally important we stay up to date with the latest scientific thinking of our international colleagues. I am very pleased to report that QBI has continued to increase the strength and calibre of its international collaborations, including the following major developments:

• QBI's already strong scientific friendship with the People's Republic of China was boosted in October 2006, when QBI neuroscientists visited Shanghai to formalise a new relationship between QBI and the Chinese Academy of Sciences, Institute of Neuroscience (ION);

• In September 2006, plans were announced to develop a Zeiss-equipped Advanced Imaging Centre – valued at more than $1.5 million – as part of the new QBI neuroscience facilities. The imaging centre will enable QBI to become the focus for the development and application of new imaging technology within the Asia-Pacific region. This represents a significant expansion of scientific ties with one of the world's most respected makers of scientific instruments. QBI and Zeiss have also agreed to create travelling fellowships to allow postdoctoral and student exchanges between QBI and the Asia–Pacific region; Zeiss is also an industry partner, underpinning the Smart State Fellowship research of QBI's Dr John Power into the cellular mechanisms responsible for emotional learning in the brain;

▲ In February 2006, a delegation led by Professor Xu Guanhua, the Minister of Science and Technology from The People's Republic of China, visited UQ for talks aimed at strengthening research ties between China and Australia.

• In August 2006, QBI organised Australia's first workshop in Mathematical and Computational Neuroscience, attended by eminent researchers from Japan, USA and Australia;

• In September 2005, QBI's inaugural Brain Plasticity Symposium attracted 25 of the world's leading neuroscientists, including Nobel Laureate Professor Susumu Tonegawa.

• In September 2004, QBI in association with SpinalCure Australia brought together five of the world's leading spinal cord researchers to discuss the latest advances in their field.

In terms of funding, QBI has received strong support through NHMRC and ARC grants, as well as Smart State funding from the Queensland Government and a $10 million allocation from the Australian Government in the 2005–06 Federal budget. Some of these funds will allow us to purchase sophisticated equipment that will enable us to expand our research into cognitive neuroscience and neuroimaging.

Targeted philanthropic funds bequeathed to QBI from the estates of community-minded patrons such as Mr Peter Goodenough, Mr

Photo: Chris Stacey, UQ

▲ Cooper Laboratory research assistant Nigel Kee inspects QBI's microarray workstation, equipment that allows scientists to analyse gene expression profiles of single cells and complex tissues.

Ross Maclean and Ms Lisa Palmer will also greatly assist in our research efforts.

The only major impediment to QBI's growth and continued success would be the failure to secure ongoing recurrent funding to ensure the retention of top scientists. The establishment of the QBI Development Board represents a major step in this direction.

QBI's interaction with the wider community is also growing. Each new QBI discovery awakens a tide of interest from the public. Accordingly, QBI plays a key role in UQ's Brain Awareness Week activities, and has extended its outreach to General Practitioners and high school students, the latter through the highly successful Australian Brain Bee Challenge – an event coordinated with the assistance of the Australian Neuroscience Society.

The past few years have also been rewarding to me beyond the establishment of QBI, since I have been awarded a Federation Fellowship from the ARC and was elected as a Fellow of the Australian Academy of Science. Both awards are a tribute to scientific colleagues with whom I have been fortunate to interact with over the years.

Finally, my sincere thanks must go to my Deputy Director (Operations) John Kelly who has provided me with outstanding administrative support and guidance over the past three years. Also, I would like to acknowledge the tremendous support and encouragement of UQ's Senior Deputy Vice-Chancellor Professor Paul Greenfield and Deputy Vice-Chancellor (Research) Professor David Siddle.

Professor Perry Bartlett FAA
Director

QBI Development Board – eight leading Queenslanders, working together to raise community awareness about neuroscience

QBI DEVELOPMENT BOARD

Bob Atkinson

Sallyanne Atkinson

Perry Bartlett

Paul Greenfield

The QBI Development Board – comprising eight leading members of the community – has been established to increase public awareness of the importance of neuroscience, and to help QBI to attract ongoing research funding.

BOB ATKINSON APM

Queensland Police Commissioner

Commissioner Bob Atkinson has had a 38-year career with the Queensland Police Service, having been sworn in as a Constable on 30 October 1968.

He has served throughout the State from Goondiwindi to Cairns, performing a wide range of operational and managerial roles. A Queensland Police Detective for about 20 years, Bob Atkinson was in charge of country Criminal Investigation Branch and Juvenile Aid offices.

He was involved in the change-management processes in the Queensland Police Force post-Fitzgerald from 1990, and then later in terms of further organisational change following the Public Sector Management Commission Review and Report Recommendations of the Queensland Police Service in 1993.

In 1989 he attended the three-month FBI National Academy Course at Quantico, Virginia, USA, a program that is aligned with the nearby University of Virginia. He again attended the FBI Academy during 2002 for the National Executive Institute Program, and holds several graduate-level qualifications.

Bob Atkinson was appointed as Commissioner of the Queensland Police Service on 1 November 2000.

SALLYANNE ATKINSON AO

BA (Hons), FAIM, AICD
Company Director and former Brisbane Lord Mayor

Sallyanne Atkinson is Special Representative for Queensland, South-East Asia in the Queensland Government. She is currently a Director of several public companies and associations and was Deputy Mayor of the Olympic Village for Sydney 2000. She is former Lord Mayor of Brisbane, Australian Senior Trade Commissioner to Paris, and Chairman of Queensland Tourism.

John Lyons

Jeff Maclean

Leigh Matthews

David Merson

As directly elected Lord Mayor of Australia's largest local authority, with a billion-dollar budget and a workforce of 7000, Sallyanne was responsible for major structural and fiscal reforms in the council and a change of image and attitude for the city of Brisbane. Internationally she has represented Australia to the International Olympic Committee and in major trade and business forums such as the OECD and the International Chamber of Commerce.

She was the leader of the Brisbane bid for the Olympics of 1992, a member of the Melbourne and Sydney Olympic bidding committee and was a founding member of the Committee to Organise the Games in 2000.

A journalist by training, she has written two books on Brisbane and numerous articles for newspapers and magazines.

PROFESSOR PERRY BARTLETT *BDSc, PhD,* FAA

Director, The Queensland Brain Institute

Following the completion of his PhD at the University of Melbourne, Professor Bartlett undertook postdoctoral studies at Johns Hopkins University, Baltimore and University College, London.

On returning to Australia, he introduced neuroscience into the Walter and Eliza Hall Institute of Medical Research.

In 2002, Professor Bartlett was appointed Foundation Chair in Molecular Neuroscience at The University of Queensland. In 2003, he was appointed inaugural Director of the Queensland Brain Institute.

His primary goal remains focused on understanding how neural stem cells regulate brain development and function, as well as defining the mechanisms by which this endogenous stem cell population can be directed toward the production of new neurons to replace those lost following disease or damage in the adult brain.

Professor Bartlett is internationally renowned in the field of cellular and molecular neuroscience, a fact highlighted by his election as a Fellow of the Australian Academy of Science (FAA) and the awarding of an ARC Federation Fellowship.

PROFESSOR PAUL GREENFIELD AO

BE PhD, BEcon, FTSE, FIChemE, FIEAust, MAIChE

Senior Deputy Vice-Chancellor

The University of Queensland

Professor Greenfield is Senior Deputy Vice-Chancellor of The University of Queensland After graduating Bachelor of Engineering, first class Honours in Chemical Engineering, from the University of New South Wales, Professor Greenfield worked in the private sector before completing a PhD at the University of New South Wales. He then worked at CSIRO before winning a three-year fellowship to the US. In 1975 he joined The University of Queensland as a lecturer in chemical engineering and a decade later became Head of Department and then Pro-Vice-Chancellor (Physical Sciences and Engineering), before being appointed as inaugural Executive Dean in 1997.

Currently, he chairs the Scientific Advisory Committee overseeing the $5.2 million Moreton Bay and Brisbane River Wastewater Management Study (since 1994), the Waste Technical Working Group, Basel Convention (since 1995), and the Advisory Board of IP Australia (since 1999). He is also a Director of several University companies including UniQuest Pty Ltd.

In 1995 Professor Greenfield won the Chemeca Medal, awarded jointly by the Institution of Chemical Engineers and the Institute of Engineers Australia for outstanding contribution to the profession. In 2006 he was named a Member of the Order of Australia for service to science and engineering, particularly through research in the areas of chemical engineering, biotechnology, wastewater and environmental management, and to the tertiary education sector.

JOHN LYONS

MBA, BBus, CPA, FAICD

Company Director and Founder of Marketshare

Founder and former chairman of Marketshare, John Lyons is now an independent company Director and businessman, with a special interest in high-growth innovative companies. He is Chairman of library technology company Softlink International Ltd, Director of O'Reilly's Rainforest Guesthouse and Canungra Valley Vineyards, and Director of on-line human resource management technology company, Onetest Pty Ltd.

John is also a Trustee and board member of the Royal Children's Hospital Foundation and of the Jupiters Casino Community Benefit Fund, and Queensland Councillor of the Australian Institute of Company Directors. He recently stepped down as Chairman of Tamawood Limited, having led the company through most of its first five highly successful years listed on the Australian Stock Exchange.

Early in his career, John Lyons topped Australia in marketing with global chemical company, Bayer. He then founded and built national market research and marketing company, Marketshare, selling it after 20 years. He is co-author with Dr Edward de Bono of the book *Marketing without Money*, which examines the "different thinking" skills of top Australian entrepreneurial innovators.

JEFF MACLEAN

Chief Executive and Executive Director
The Index Group

Jeff is CEO and Executive Director of the Index Group of Companies, a family-owned, diversified group of small businesses operating from Carole Park in Brisbane. The Index Group is well placed in the Queensland Business Review Q400 – the top 400 privately owned businesses in Queensland.

Index's business operations include sales of used crushing and quarrying equipment, supply of commercial water treatment plants, industrial property, processing high quality silica sand which is exported for LCD glass production, and the breeding and racing of thoroughbred horses.

Before working with Index, Jeff introduced Kreepy Krauly (automatic pool cleaners) into the Queensland market in 1977, owning and operating that business for more than 20 years.

Apart from a brief association with the Index Group in the mid-1970s, it was not until the mid-1990s that Jeff returned to the family company to work at his father's side once more. After selling the pool cleaner business in 1998, Jeff was able to concentrate his efforts fully on Index. In February 2005, Jeff's father – Ross Maclean – passed away from motor neuron disease and Jeff continues the day-to-day management of the Index businesses.

Jeff is currently also the Chair for the Commercial Division of the Salvation Army Brisbane Appeal Committee.

LEIGH MATTHEWS

Coach Brisbane Lions
and Motivational Speaker

One of Australia's most recognised and respected sporting identities, Leigh Matthews has matched his well-documented success as a player with an equally notable career as coach, motivator and mentor.

Known for his straight talking and mental toughness, Leigh has learnt from long experience how to achieve goals and inspire others to do the same.

As an Australian Football League player for Hawthorn from 1969–85, he was a member of four premiership sides and was premiership captain in 1983. He coached Collingwood from 1986 to 1995, for five finals appearances, and in 1990 took the club to its first premiership since 1958.

In 1998, Leigh was lured out of 'retirement' to re-join the roller-coaster ride of AFL coaching. Realising he missed the weekly challenge of the game he admits has been his 'thing' throughout his life, he accepted a three-year contract as senior coach with the Brisbane Lions.

At the Lions, Leigh Matthews has created one of the powerhouse teams in the AFL, taking the team to their first grand final in 2001, followed by back-to-back premierships which saw the Lions win the grand final again in 2002. He then became a part of true football history in 2003, winning his third premiership in a row.

As well as coaching high-profile sporting teams, Leigh is often called upon to share his brand of leadership with the business world as a speaker and motivator.

DAVID MERSON

BEcon, BE

Company Director and Founder of Mincom Ltd

David Merson is a graduate in Electrical Engineering and in Economics from The University of Queensland. Since 1966 he has worked in the information technology industry in Australia and Europe.

In 1979 he founded Mincom Limited, and was its CEO until 2000. During his tenure, Mincom grew to be Australia's largest software developer and exporter, with revenue of $200 million, 1300 staff, 20 offices around the world, and global leadership in several software categories.

Since retiring from Mincom, David has become a Director of a range of organisations, including Australian software companies, research institutes and charitable institutions.

His achievements have been recognised with an Honorary Doctorate in Engineering from The University of Queensland, a Centenary Medal from the Australian Government, the Export Hero award from the Australian Institute of Export, the inaugural Australian Information Technology Association's Gold award, and the inaugural CSIRO iAward for individual achievement in the IT industry (2005).

RESEARCH FELLOWSHIPS

Professor Perry Bartlett
Australian Research Council (ARC) Federation Fellowship

Dr Paul Beatus
Swedish Cancer Society Postdoctoral Fellowship

Dr Elizabeth Coulson
National Health and Medical Research Council (NHMRC) RD Wright Fellowship

Dr Andrew Delaney
ARC Australian Postdoctoral Fellowship

Dr Louise Faber
NHMRC RD Wright Fellowship

Dr Dhanisha Jhaveri
Human Frontier Science Program Long-term Fellowship

Dr Li Li
NHMRC Peter Doherty Fellowship

Dr Michael Piper
NHMRC Howard Florey Centenary Research Fellowship

Dr John Power
Queensland Government Smart State Fellowship

A/Prof. Linda Richards
NHMRC Senior Research Fellowship Level B

Dr Rod Rietze
Pfizer Australia Senior Research Fellowship

Dr Robyn Wallace
QBI Ross Maclean Research Fellowship

PRIZES AND AWARDS

QBI DIRECTOR NAMED AUSTRALIAN ACADEMY OF SCIENCE FELLOW

In March 2003, Professor Perry Bartlett was honoured by election to the Australian Academy of Science. Election to the Academy as a Fellow recognises a career that has significantly advanced the world's scientific knowledge.

Professor Perry Bartlett

2006 Paxinos Watson Prize for the most significant neuroscience paper published by a full member of the Australian Neuroscience Society in the previous full calendar year – 2004 *Journal of Neuroscience* paper (Y Goldshmit, MP Galea, G Wise, PF Bartlett & AM Turnley: Axonal regeneration and lack of astrocytic gliosis in EphA4-deficient mice).

Professor Pankaj Sah

2005 Australian Neuroscience Society's and Neurosurgical Society of Australasia's Eccles Lecturer.

Dr Elizabeth Coulson

2004 AW Campbell Award for "The best contribution by a Member of the Australian Neuroscience Society in their first five postdoctoral years".

Dr Rod Rietze

UQ Foundation Research Excellence Award – grant in recognition of early career excellence.

Dr Dhanisha Jhaveri (Bartlett lab)

2003 Indian National Science Academy's Medal for Young Scientists (presented to 15 of the country's best and brightest in science and technology).

Tom Keeble (Cooper lab)

Tom shared the 2006 Istvan Törk Prize for the best oral presentation by a student member of the Australian Neuroscience Society. The ANS recognised Tom's work on the role of the Wnt receptor Ryk in axon guidance. These studies featured in a 2006 *Journal of Neuroscience* paper (The Wnt receptor Ryk is required for Wnt5a-mediated axon guidance on the contralateral side of the corpus callosum – Keeble *et al*).

Maricar Sy (Rietze lab)

2005 Australian Neuroscience Society Student Poster Prize – for Honours project.

Dr Alan Woodruff (Sah lab)

In 2004, Alan won both the Sir Grafton Elliot-Smith Award for the best essay on a neuroscience topic by a student member of the Australian Neuroscience Society (GABAergic interneurons and the control of rhythmic activity) and a Student Poster Prize (for his work on the inhibitory neural circuitry of the amygdala). Alan graduated in July 2006 and has taken up a postdoctoral position with Professor Rafael Yuste at Columbia University, where he will apply his expertise to the investigation of cortical microcircuitry.

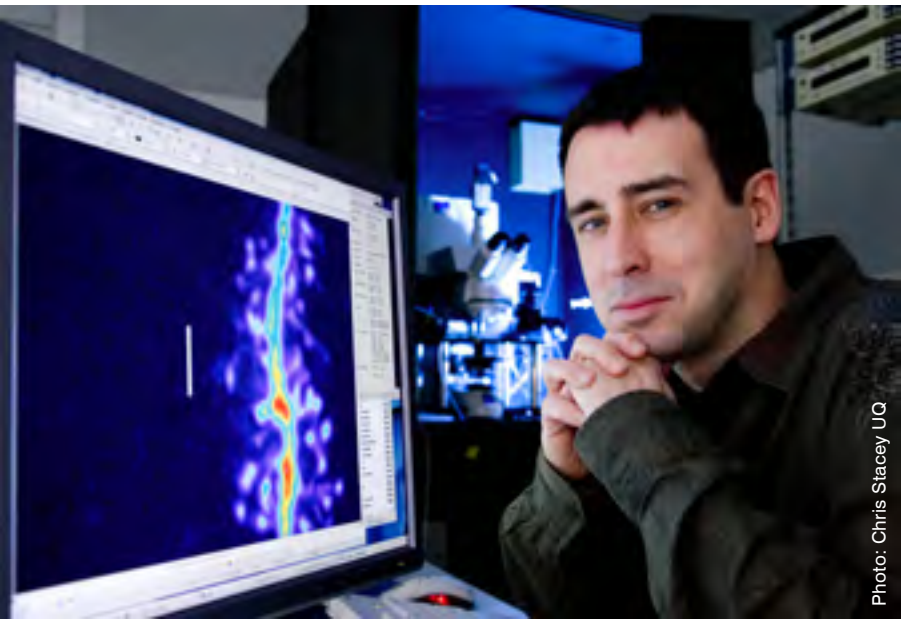
"Working with Zeiss to improve and develop microscope design will have a raft of benefits for Queensland and Australia."
– Dr Power

SMART STATE FELLOWSHIP
AWARDED TO QBI SCIENTIST

Collaboration between The University of Queensland and world-renowned microscope maker Carl Zeiss took another leap forward in 2006 when the Queensland Government awarded a three-year $150,000 Smart State Fellowship to QBI Research Fellow Dr John Power. The grant will enable Dr Power to continue his research into the cellular mechanisms responsible for emotional learning in the brain using advanced microscope technology.

"I'll be looking at changes that are occurring within the cells of the amygdala, part of the brain that has particular relevance for anxiety disorders," Dr Power said.

Amygdala dysfunction has been implicated in a range of anxiety disorders, including post-traumatic stress and addiction.



▲ Queensland Government Smart State Fellowship winner Dr John Power is looking at changes that occur within the cells of the amygdala.

A key part of Dr Power's fellowship will be collaboration with Zeiss Australasia in developing new imaging technologies, a move which has long-term implications for Australian neuroscience.

"Working with Zeiss to improve and develop microscope design will have a raft of benefits for Queensland and Australia," Dr Power said.

Until recently, high-resolution laser scanning confocal microscopy has been designed primarily for physicists and anatomists who use fixed tissue, not for high-speed imaging of living neurons.

"As it's a rapidly developing field, neuroscience has particular technological needs," Dr Power said.

"Put simply, living cells don't like to be subjected to lasers, so we have to come up with new ways of mapping and observing what's happening in the amygdala – as well as other parts of the brain.

"By working closely with Zeiss, we'll be able to develop systems that meet our need to capture images of live cells."

"Collaboration with Zeiss will ultimately mean early access to state-of-the-art technology in Queensland."

Dr Power completed his PhD in Chicago in 1999. He is currently a Research Fellow in Professor Pankaj Sah's laboratory.

RESEARCH GRANTS

RESEARCH GRANTS 2006

Bartlett PF, Boyd AW, Hallahan AR, Reynolds BR, Rietze RL, Vescovi AL, Walker DG, Wainwright BJ (2006) Australian Cancer Research Foundation, Equipment Grant for a Brain Tumour Research Centre; $1,114,000

Bartlett PF (2006–2013) Department of Health and Ageing QBI — Medical Research Infrastructure (2006); $10,000,000

Breakspear MJ, Morley JW, Harris JA, Sammut CA, Goodhill GJ, Paxinos G, Lovell NH, Knock SA, Lagopoulos J, Malhi GS, Macefield V (2006–2011) ARC/NHMRC Thinking Systems Grant: Optimizing autonomous system control with brain-like hierarchical control systems; $3,300,000

Faber ESL (2006–2010) NHMRC RD Wright Biomedical Career Development Award; $479,875

Gonda TJ, Gabrielli BG, Grimmond SM, Barry PF, Bartlett PF, Whitehead JP, Crossley M, RW Johnstone, Musgrove EA (2006) ARC LIEF Grant: A facility for high throughput,

QBI RESEARCHER WINS TOP INDIAN SCIENCE AWARD

In October 2003, Dr Dhanisha Jhaveri (right) was awarded one of India's top awards for young scientists.

A postdoctoral fellow, Dr Jhaveri was presented with the Indian National Science Academy's Medal for Young Scientists in Delhi.

This prestigious award is presented to only 15 of the country's best and brightest young scientists in the area of science and technology each year.

Dr Jhaveri said the award was quite an honour.

"It means a lot to me and my family in terms of the work that I have put in and to know what the results are," she said.

Dr Jhaveri completed her PhD at the Tata Institute of Fundamental Research in Mumbai and came to The University of Queensland on a Long-term Human Frontiers Science Program Fellowship.

At QBI she has been looking into how stem cells in the brain are regulated with a view to producing new neurons.

QBI Director, Professor Perry Bartlett said he was proud to have someone of Dr Jhaveri's talent at the Institute.

"This is an incredibly prestigious award and it shows we are attracting the best people from around the world," Professor Bartlett said.

functional gene discovery using arrayed retroviral expression cloning; $824,610

Goodhill GJ (2006–2008) ARC Discovery Grant: Wiring up the nervous system: how do axons detect molecular gradients?; $341,000

Lewis RJ, Hooper JD, Pountney DL, Hancock JF, Capon RJ, Waters MJ, Minchin R, Reynolds BA, Timms P, Bottle SE, Clements JA, Johnson NW (2006) ARC LIEF Grant: Biomolecular discovery and analysis facility; $542,000

López JA, Reynolds BA, Lakhani S, Schmidt C (2006–2007) National Breast Cancer Foundation Concept Award: Mammospheres for immunotherapy; $150,000

Piper MJ (2006–2008) NHMRC Howard Florey Centenary Research Fellowship: The role of Nfi genes in development of the corpus callosum; $172,500

Power JM (2006–2008) Queensland Innovation Skills Fund Smart State Fellowship: Calcium dynamics in the amygdala neurons; $150,000

Reynolds BA, Bartlett PF, Rietze RL, Osborne GW (2006–2007) Australian Stem Cell Centre Grant: Platform technologies for the isolation and identification of adult and embryonic stem cells and their progeny; $212,000

▲ Briony Fox – a research assistant in the Coulson Laboratory.

Richards LJ (2006-2010) NHMRC Senior Research Fellowship Level B; $642,125

Richards LJ (2006–2008) NHMRC Project Grant: Regulation of cortical development by Nfi genes; $509,025

Richards LJ, Goodhill GJ, Bartlett PF, Koopman PA, Wainwright BJ, Smith MT, Mackay-Sim A, Kilpatrick T (2006) ARC LIEF Grant: Advanced cell labelling and imaging facility; $400,000

Wiles JH, Bartlett PF, Burrage K, Goodhill GJ, Mattingley JB, Sah P, Smith AE, Srinivasan MV, Wyeth GF, Arbib MA, Elman JL, O'Keefe JM (2006–2011) ARC/NHMRC Thinking Systems Grant: Thinking systems: navigating through real and conceptual spaces; $3,300,000

RESEARCH GRANTS 2005

Bartlett PF, Boyd AW, Turnley AM, Galea MP (2005–2008) SpinalCure Australia Lisa Palmer Spinal Research Consortium; $650,000

Boyd AW, Bartlett PF, Turnley AM, Galea MP (2005–2007) NHMRC Project Grant: Is EphA4 the major molecular regulator of axonal regeneration?; $483,500

Delaney AJ, Faber ESL, Sah P (2005–2007) NHMRC Project Grant: Excitatory synaptic circuitry and plasticity in the amygdala; $399,750

Goodhill GJ (2005) National Institutes of Health (USA) CRCNS: Mechanisms of axonal gradient detection; $18,857

Grimmond SM, Koopman PA, Perkins AC, Hume DA, Little MH, Bertram JF, Aitken RJ, Cooper HM (2005) ARC LIEF Grant: Developmental imaging facility; $441,100

Photos: Chris Stacey, UQ

▲ Quality Control Manager Mary White supervises tissue-culture procedures across the Institute, an essential part of quality control and scientific best-practice.

Lu G, Cooper HM, Xu ZP (2005–2007) ARC Discovery Grant: Tailoring of layered double hydroxide nanoparticles for effective delivery of biologically active peptides and cDNAs; $499,254

Quinn RJ, Mackay-Sim A, Rietze RL (2005) ARC LIEF Grant: Queensland high-throughput confocal cell imaging facility; $578,145

Richards LJ (2005–2006) National Institutes of Health (USA): Neurons in the subcallosal sling; $273,101

Richards LJ (2005–2008) March of Dimes Birth Defects Foundation Grant: Signalling of Slit2 in corpus callosum development; $217,241

Wallace RH (2005–2007) The Index Group: Ross Maclean Senior Research Fellowship; $200,000

RESEARCH GRANTS 2004

Bartlett PF, Tan SS, Kilpatrick TJ, Sah P (2004–2008) NHMRC Program Grant: Regulation of neural cell production in the normal and diseased brain; $6,474,750

Bartlett PF *et al.* (2004) ARC Research Networks Seed Funding: A neural network: understanding brain function; $10,000

Bull ND (2004–2005) Australasian Spinal Research Trust Perry Cross Fellowship; $80,000

Cooper HM (2004–2006) NHMRC Project Grant: Dissecting the molecular mechanism driving neuronal migration triggered by the Netrin receptor, Neogenin; $425,250

Coulson EJ (2004–2008) NHMRC RD Wright Biomedical Career Development Award: Molecular mechanisms of neuronal cell death in the adult; $437,500

Coulson EJ (2004–2006) NHMRC Project Grant: Proteolytic cleavage of the p75 neurotrophin receptor mediates cell death; $234,750

Delaney AJ, Sah P (2004–2006) ARC Discovery Grant (with Australian Postdoctoral Fellowship): Characterisation of monoaminergic transmission in central amygdala; $260,016

Goodhill GJ (2004–2006) University of Pennsylvania (USA) CRCNS: Spontaneous activity, lateral interactions and cortical maps; $237,000

Jhaveri D (2004–2006) Human Frontier Science Program Long-term Fellowship: Regulation of neural stem cell differentiation in the mouse brain; $117,716

Li L (2004–2007) NHMRC Peter Doherty Australian Postdoctoral Fellowship: Genetic study on activation of adult neural stem cells after ischaemic stroke; $289,000

Rietze RL (2004–2008) Pfizer Australia Senior Research Fellowship: Neuronal production in the adult brain; identification of the factors which regulate the activity of the endogenous stem cell population; $983,562

Rietze RL (2004–2006) NHMRC Project Grant: Identification and origin of neuronal precursors in the adult mouse hippocampus; $280,500

Sah P, Bartlett PF, Vaney DI, Adams DJ, Learmonth RP (2004) ARC LIEF Grant: The Centre for Advanced Light Microscopy: equipment for *in vivo* multiphoton microscopy and high-throughput confocal microscopy; $321,456

RESEARCH GRANTS 2002–2003

Bartlett PF (2002–2003) NHMRC Senior Principal Research Fellowship; $235,500

Bartlett PF (2003) NHMRC Project Grant (transfer from BFI Grant): Central nervous system and neurogenetics; $227,836

Bartlett PF (2003–2008) ARC Federation Fellowship: Cellular plasticity in the brain: discovering molecular mechanisms controlling the production of neurons during brain development, function, ageing and disease; $1,481,765

Bartlett PF, Bellamy M, Coulson EJ, Rietze RL (2003) Centre of National Research on Disability and Rehabilitation Medicine Collaborative Grant: Molecular mediators of traumatic damage: targets for drug therapy; $250,000

Bartlett PF, Mackay-Sim A, Herington A, Adams DJ, Pettigrew JD, Key B, Noakes P, Bellingham M, Nurcombe VA (2003) ARC LIEF Grant: A cell sorter facility for neuroscience and related biotechnology; $511,824

Beatus P (2002–2004) Swedish Cancer Society Postdoctoral Fellowship; $156,000

Cooper HM (2003) NHMRC Project Grant (transfer from BFI Grant): Protein targeting and signal transduction; $168,164

Coulson EJ (2001–2003) Motor Neuron Disease Research Institute of Australia Sealey Research Fellowship; $270,000

Rietze RL (2002) Australasian Spinal Research Trust Grant: Stem cells and spinal cord repair; $25,000

Rietze RL (2003) Motor Neuron Disease Research Institute of Australia Grant: Stimulation of endogenous stem cells to replace motor neurons; $28,411

Sah P (2001–2003) Pfizer Australia Grant: Molecular and physiological identification of a novel GABA receptor in the amygdala; $610,000

Sah P (2003) NHMRC Project Grant: Excitatory synaptic circuitry and plasticity in the amygdala; $150,000

SECTION TWO

2

QBI researchers are investigating the mechanisms that drive neurogenesis, a brain function which holds the key to the development of new therapies for neurodegenerative disorders and maintenance of mental health.

QBI NEUROSCIENCE

"Until a decade ago, it was generally accepted that the generation of new nerve cells in the central nervous system did not persist into adulthood."

– Professor Perry Bartlett

BARTLETT LABORATORY

At QBI, we believe the brain's ability to make new connections and even new nerve cells is the basis of important functions such as learning and memory. Understanding the regulation of these processes offers the promise not only of promoting life-long cognitive health, even in the older population, but also of developing a new generation of therapeutics to treat the avalanche of neurological and mental conditions that accounts for almost half of the disease burden of our community.

Professor Perry Bartlett *BDSc, PhD, FAA*

Adrian Carter, *BSc (Hons)*
Amanda Hammond, *BSc*
Debra Black, *BSc (Hons)*
Dhanisha Jhaveri, *BSc, MSc, PhD*
Fiona Rogers, *BA/BSc (Hons)*
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Li Li, *MSc, MBBS, PhD*
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Nicola Watts, *BPsych (Hons)*
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Tara Walker, *BApp Sci, PhD*
Ying Zhang, *BSc, MSc, PhD, ACRP*

In 1992, the Bartlett laboratory, primarily through the work of current QBI scientist Linda Richards, reported the presence of a population of neural precursors, or stem cells, in the adult brain that had the propensity to produce new neurons. This discovery was followed in 2001 by a front-cover article, primarily from the work of QBI scientist Rod Rietze, in the leading research journal *Nature,* reporting the isolation and characterisation of the previously identified self-renewing population of stem cells.

These discoveries provided tangible evidence for the most significant discovery in neuroscience in decades: that the brain and spinal cord possess the same powers of self-renewal and repair as other major organs and tissues. This neurogenesis underpins neural plasticity – the brain's ability to form new connections and regain function after traumatic injuries, stroke or neurodegenerative damage.

Since then, the Bartlett laboratory has been investigating the molecules that regulate the

production of new neurons in two regions of active neurogenesis: the hippocampus, which mediates memory storage, and the olfactory bulb, locus of the sense of smell. It is known that environmental stimuli trigger bursts of synaptic activity that activate neurogenesis and, by stimulating neural stem cells *in vitro* with methods that mimic synaptic activity, the Bartlett laboratory induced stem cells to divide and form neural precursor cells.

In addition, the Bartlett laboratory is investigating how external stimuli are transduced as molecular signals that stimulate and regulate neurogenesis. Using micro-arrays to analyse gene expression patterns in neural stem cells, they showed that neural stem cells express the p75 neurotrophin receptor (p75NTR). Subsequently they have shown that brain derived neurotrophic factor (BDNF) stimulates neurogenesis through this receptor.

Flow cytometry using p75NTR as a marker has allowed the purification of stem cells from the adult brain, revealing one of the first positive markers for the isolation of neural stem cells. Recently, the laboratory has shown that BDNF acts both as a mitogen, stimulating stem-cell division, and as a differentiation factor. It appears to drive stem cells to form neural precursors, and then shapes neural precursors into fully differentiated neurons. Neural stem cells also express receptors for two closely related signalling molecules with multiple roles in the body, leukaemia inhibitory factor (LIF), and oncostatin M (Osm). Both LIF and Osm have cytokine-like activity in the brain, consistent with their known role in early brain development in the embryo. In knockout mice lacking Osm receptors, only 50 to 60 per cent of neural precursor cells differentiate into neurons, and the number of neural precursors increases proportionally. Osm appears to inhibit terminal differentiation of neural precursors.

Neural stem cells also express receptors for the cytokine interferon gamma (IFNγ), which, in addition to its regular role as an inflammatory agent, appears to strongly inhibit differentiation of the stem cells into neural precursors. This finding is intriguing, given that specialised immune-system cells in the brain, called microglia, secrete high levels of IFNγ, that cause local inflammation after a stroke, injury or toxic insult. In addition, IFNγ-mediated inflammation strongly suppresses production of neural precursors. These effects of IFNγ offer a possible explanation for how external factors such as head injury or stroke, which result in inflammation, may inhibit neurogenesis.

▼ **Bartlett Lab: (L–R from page 32)** Amanda Hammond, Sumiti Saharan, Fiona Rogers, Dhanisha Jhaveri, Paul Beatus, Perry Bartlett, Ying Zhang, Briony Fox, Debra Black, Tara Walker, Geoffrey Turnbull, Nicola Watts, Li Li, Takahiro Yasuda, Adrian Carter, Michael Colditz, Ying Wang

The Bartlett laboratory is also involved in a major collaborative project with UQ's Professor Andrew Boyd and researchers from the University of Melbourne

The Bartlett laboratory is also involved in a major collaborative project with UQ's Professor Andrew Boyd and researchers from the University of Melbourne. This work seeks to stimulate regrowth of axons to repair the spinal cords of individuals with crippling spinal-cord injuries. The project is focused on EphA4, a molecule that appears to inhibit regeneration of severed axons. Six years ago, the research team developed transgenic EphA4-knockout mice whose axons regrew through spinal-cord lesions and formed enough new connections to restore some movement to the animals. In normal mice, the severed axons retreat about 2 mm from the midline of the lesion site, and then attempt to grow back. However they fail to cross the lesion site and form new connections. EphA4 is highly expressed by injured spinal-cord neurons, but it was not clear whether it blocked or promoted regrowth. In the EphA4-knockout mice, 70 per cent of the severed axons grew straight through the lesion – the first time that something more than perfunctory axonal regrowth had been demonstrated in spinal cord injury. It now appears that EphA4 acts to inhibit the regrowth of damaged axons by forming a repellent barrier at the site of injury.

The research team has more recently identified several compounds that effectively inhibit EphA4 activation so that axons readily grow through the site of the lesion. At present work is proceeding to identify the most promising inhibitor to take to clinical trials in the next few years.

The Australian Cancer Research Foundation (ACRF) has backed The University of Queensland's move to develop a tumour cell testing facility at the Queensland Brain Institute (QBI).

The $1.14 million centre will be the world's first automated 'high-throughput' screening facility designed for testing and identifying stem cells derived from human brain tumours.

QBI Director, Professor Perry Bartlett said the facility would help scientists to develop more effective treatments for brain cancer.

"This is the first time researchers will be able to isolate, enumerate and purify tumour stem cells with such high levels of efficiency," Professor Bartlett said.

"We know brain cancer occurs in about 10 in every 100,000 people in the Western world. It's a disease that presents in patients of all ages, and is the second most common tumour type among children and young adults."

Despite significant advances in treatments, the average life expectancy of patients with aggressive forms of brain cancer is often less than a year.

Resistance to treatment is related to the slow rate of division of the tumour cells, as well as their migratory nature and ability to integrate themselves into normal neural tissue.

Crucially, some adult neural stem cells have similar characteristics to brain cancer cells – which is why QBI neuroscientists are eager to learn more about them.

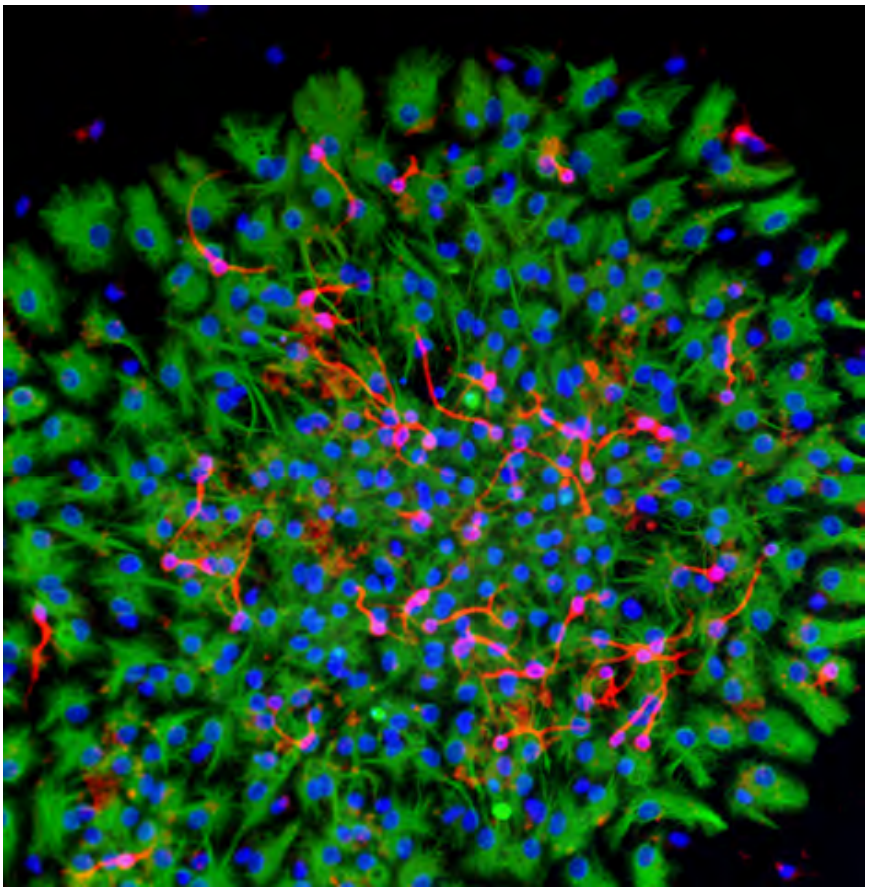
"There is an emerging view among neuroscientists that cancers in the central nervous system may contain a population of stem cells that may be responsible for tumour initiation and malignancy," Professor Bartlett said.

"Until now, one of the primary difficulties in studying these stem cells was that scientists lacked the tools to identify and collect them."

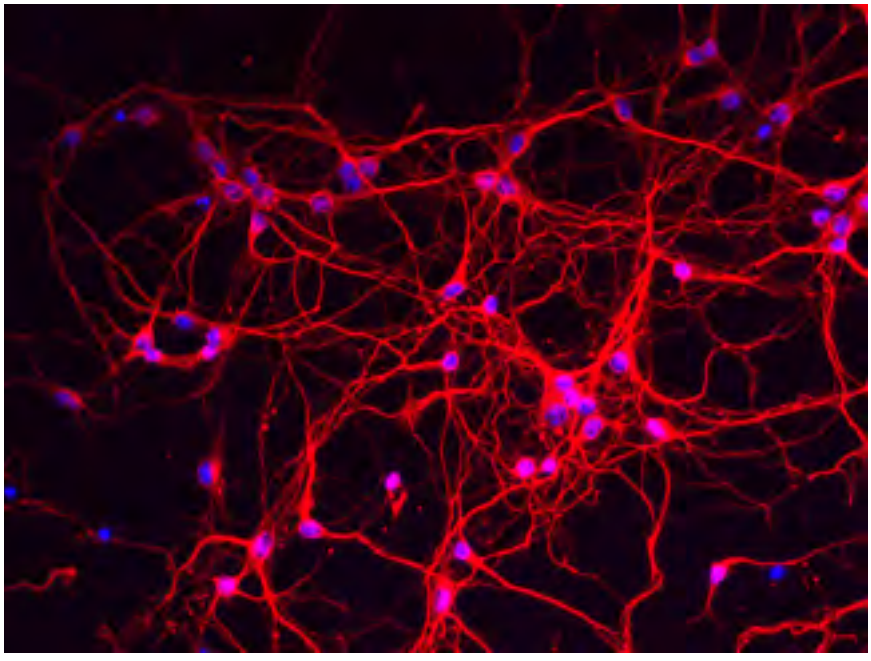
The new screening facility uses a combination of advanced techniques to record molecular changes in neural stem cell assays.

Scientists from QBI, the Institute for Molecular Bioscience and the Queensland Institute for Medical Research, as well as research clinicians from Brisbane's leading public hospitals, will all have access to the ACRF Brain Tumour Research Centre.

Australian Cancer Research Foundation



Primary hippocampal neurosphere grown in the presence of mitogens, part of QBI research which featured on the cover of the Journal of Neuroscience in December 2005.



Doublecortin-positive neurons from the brain of a 14-day-old mouse.

" We are constantly striving to develop new methods and techniques that allow us to better study and understand precursor activity in the mammalian brain."

– Professor Brent Reynolds

REYNOLDS LABORATORY

The Reynolds laboratory is focused on investigating the role precursor cells play in normal brain function, and in states of injury and disease. Our approach to understanding this problem is diverse and ranges from the development of new technologies to identify and measure precursor activity and screening of compound libraries, through to translational therapeutic development via transplantation of exogenous progenitors and the *in vivo* activation and deactivation (in the case of cancer stem cells) of endogenous precursors. In general, there are three major research streams:

1. NEW TECHNOLOGIES

Science is often driven by the development of new technologies where being able to see, do or change things has given new insight into function or uncovered previously undetected biological processes. There are numerous examples of technologies that have influenced our understanding of the world and the development of new technologies may well be the single most important contributor to scientific advancement. In this light, we are constantly striving to develop new methods and techniques that allow us to better study and understand precursor activity in the mammalian brain. We have or are in the process of developing the following:

i. Neural Colony Forming Cell Assay (N-CFCA) – In collaboration with StemCell Technologies (Vancouver, Canada) we have developed and launched a new assay that provides a more accurate measure of stem and progenitor cell frequency in comparison to the currently used method (Neurosphere Assay – NSA). Until development of the N-CFCA it was commonly believed that the NSA gave a meaningful read-out of neural stem cell activity. However, re-analysis of the use of the NSA revealed that, while the assay does measure precursor frequency, it cannot distinguish between stem and progenitor cells (Reynolds & Rietze, 2005, *Nature Methods*). The N-CFCA allows this distinction to be made and has proved valuable in analysing stem cell activity *in vivo* and *in vitro* (Bull & Bartlett, 2005, *Journal of Neuroscience*). We are currently adapting the culture conditions so the assay can be used to measure stem cell frequency in cells derived from human brain tumours.

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Amy Dedman, *BBiotech (Hons)*
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Jesse Johnson, *BSc*
Jonathon Robson, *BSc (Hons)*
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Louise Colclough, *BSc*
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ii. Mathematical Modelling of Stem Cell Activity – It has been proposed that mathematics will be the new microscope for the 21st century, allowing us to see biological processes that cannot be seen by any other means. In collaboration with Geoff Ericksson (QBI), Kevin Burrage (UQ School of Physical Sciences) and Rod Rietze (QBI) we have developed and tested an algorithm that allows us to measure the frequency of symmetric stem cell divisions using data generated from cells passaged in the NSA. The model has been applied to studying the effects of growth factors, gene deletions and age on somatic stem cell proliferation and has been instrumental in the discovery of molecules that regulate tumour stem cell proliferation (Piccirillo *et al.*, 2006, *Nature*).

iii. Flow Cytometry Multiplex High Content Phenotyping – Together with Geoff Osborne (Director, QBI Flow Cytometry Facility) and the Australian Stem Cell Centre, we are developing an antibody-screening platform that will allow us to phenotype the antigenic profile of any given cell population and to apply a large panel of antibodies to the isolation of distinct and rare populations of cells. Our antibody-screening platform uses a semi-automated robotic-assisted workstation together with multispectral antibody analysis to effectively access the binding characteristics of large combinations of antibodies and to ultimately apply this to the sorting of specific cell populations. We are applying this technology to the identification of somatic stem cells and unique progenitor populations, in addition to the hunt for the tumour-initiating or cancer stem cells.

2. CANCER STEM CELLS

Within the past few years, the cancer stem cell hypothesis has gained significant momentum based on the demonstration of small populations of cells within blood and solid tissue tumours that not only exhibit stem cell characteristics but also are responsible for tumour-initiating and possibly long-term growth. The attractiveness of this concept is that it may provide an explanation for why many of our current cancer treatments are ineffective and, in addition, provides a new and potentially more relevant therapeutic target. We have been applying our considerable expertise in somatic neural stem cells to the study of cancer stem cells, and have several on-going projects that dovetail with some of the new technologies that the laboratory is developing.

i. Identification of CNS Tumour-Initiating/ Cancer Stem Cells – Due to the inherent heterogeneity and the promiscuous morphology of many brain tumours, morphological classification can often be difficult. Hence, there is growing consensus that molecular genetic analyses will soon become important to improve classification

▼ **Reynolds Lab: (L–R)** Hassan Azari, Loic Deleyrolle, Nissa Carrodus, Amy Dedman, Maria Caldeira, Brent Reynolds

"Our goal is to determine the cells that are responsible for tumour initiation and growth, and to further study the cellular and molecular characteristics of this population."

of various glioma subtypes. While this approach is a natural evolution based on the development of new technology, one may argue that its application, while a valuable addition to the currently used method, suffers from the same inherent flaw as morphological classification – namely categorisation based on a population analysis. The majority of cells within the tumour population dominate the final histological and molecular characterisation. As tumours are composed of a heterogeneous population of cells, of which a small percentage appear able to initiate and sustain tumour growth (i.e. the tumour-initiating cells), basing tumour classification on an analysis of the tumour-initiating cell population may provide not only an additional classification criterion but also a potential prognostic and/or diagnostic tool for therapeutic development.

Using our antibody-screening platform and automated sphere-counting algorithm (developed by Geoff Ericksson), we are actively hunting for the tumour-initiating cell(s) in tumours derived from paediatric and adult brains. Our goal is to determine, based on antigenic phenotyping, the cells that are responsible for tumour initiation and growth and to further study the cellular and molecular characteristics of this population by testing the effects of exogenous signalling agents and by gene array analysis, respectively.

This research program involves collaboration with several clinical groups (Adrian Nowinske, Princess Alexandra Hospital; David Walker, Royal Brisbane Hospital) and basic research laboratories (Bryan Day, Queensland Institute of Medical Research; Angelo Vescovi, University of Milan; Bjorn Schefler and Dennis Steindler, McKnight Brain Institute, University of Florida; Harley Kornblum, University of California Los Angeles; Sharon Louis, StemCell Technologies, Vancouver).

ii. Identification of Breast Tumour-Initiating/Cancer Stem Cells

Complementing our brain tumour research program is a similar project focused on identifying and isolating a breast cancer tumour-initiating/cancer stem cell(s). The recent demonstration of the growth and expansion of breast tumour cells using the Neurosphere Assay conditions has encouraged us to apply the technology we have developed for studying brain tumour-initiating cells to breast cancer. As for our central nervous system tumour stem cell project, we are using the Flow Cytometry Multiplex High Content Screening platform to identify and enrich for breast tumour-initiating cells and will further characterise this population using molecular and cell signalling analysis. This project is in collaboration with researchers at the Queensland Institute of Medical Research, with a particular focus on the metastatic tumour-initiating cell(s) (Sunil Lakhani) and the use of these cells in dendritic cell therapy (Chris Schmidt and Alejandro Lopez).

3. CELL REPLACEMENT

The loss of neurons following injury or disease necessitates their replacement. There are currently two strategies to achieve this: i) transplantation of exogenous precursor cells and ii) activation of endogenous stem and progenitor cells. We are actively pursuing both approaches.

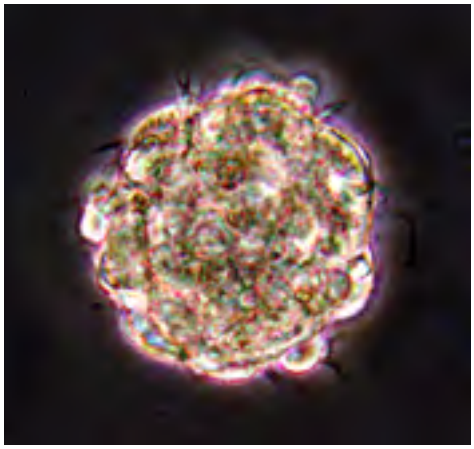
i. Transplantation of Stem Cell-Derived Progeny – The principal approach over the past 30 years to replacing cell loss in the central nervous system has been via implantation of donor-derived progenitors. While the transplantation field began using primary foetal tissue as the source for donor cells, the development of methodologies to isolate and expand neural stem cells and recently human embryonic stem (hES) cells provides a more realistic option for a reliable and plentiful source of donor cells, in addition to a choice that is more ethically acceptable. One of the shortcomings of using neural stem cells, and a significant

problem for its practical application, is the relatively low yield of neurons. To overcome this problem we have, in collaboration with the Steindler laboratory at the University of Florida, developed a methodology to obtain a highly enriched (more than 90 per cent) neuronal population. We are characterising this population *in vitro* and following implantation, in addition to testing its applicability in several animal models.

Similarly, a problem can exist with ES cells where less than 50 per cent of the progeny differentiate into neurons. Not only should our enrichment procedure help to obtain a more purified and reliable source of donor cells from this source, but it will also allow for the negative selection of undifferentiated cells that may be responsible for tumour formation.

ii. Activation of Endogenous Precursors – The existence of stem cells throughout the ventricular neuraxis of the adult mammalian central nervous system (Weiss *et al*., 1996, *Journal of Neuroscience*), and their ability to respond to mitogenic activation (Craig *et al*., 1996, *Journal of Neuroscience*) and injury, raises the possibility that central nervous system injury and degeneration can be repaired via activation of endogenous precursor cells. We are currently pursuing strategies to activate stem cells and their progeny so as to replace or protect cells lost, or susceptible, to injury or degeneration. In regards to this approach, we are using the following models – stroke, Huntington's disease (R6/1-2), motor neuron disease (SOD-1 rats and mice) and spinal cord injury.

While the application of endogenous stem cell progeny to address issues of cell loss in models of injury and disease is fairly obvious, the role that stem cells play in ageing is less so. To this end, we are collaborating with Rod Rietze (QBI) and have found that stem cell (in line with progenitor cell) numbers are reduced in the ageing subventricular zone, and that this reduction can be partially reversed by activating stem cell division with growth hormone. The effect this may have on age-related cognitive decline and susceptibility to degeneration is being pursued.



▲ Tumorsphere – a phase contrast image of a tumorsphere derived from an adult human glioblastoma multiforme tumour stem cell.

"Until recently, the neurosphere assay (NSA) was considered to be a reliable and robust read-out of stem cell activity."
– Dr Rod Rietze

RIETZE LABORATORY

The focus of our lab is to understand, at a molecular and cellular level, how endogenous adult mammalian neural stem cells (NSCs) are regulated, so as to harness their regenerative capacity and ultimately prevent or restore cognitive function lost due to ageing or disease. As such, our work is focused on four main areas: a) the development of novel assays to discern stem cells from more differentiated progeny *in vitro* and *in vivo*, b) the phenotypic characterisation of adult NSCs and their progeny, c) determining the effects of growth hormone signalling on the regulation of endogenous NSC function, and d) characterisation and prevention of age-related declines in endogenous NSCs.

1. ASSAY DEVELOPMENT

i. Neural Colony Forming Cell Assay
As part of an active collaboration with the Reynolds lab (p 24) and Dr Sharon Lewis (StemCell Technologies, Vancouver, Canada), we assisted in the validation of a novel *in vitro* assay which enables the discrimination of stem from more differentiated progenitor cells. This represents a major technological advance that will have a significant impact not only in developmental and regenerative neurobiology, but also in other areas of tissue-specific stem cell research.

ii. Mathematical Modelling of Stem Cell Activity
In collaboration with Professor Kevin Burrage (Advanced Computational Modelling Centre, UQ), Dr Geoff Ericksson (QBI) and Professor Brent Reynolds (QBI), we have developed a mathematical algorithm that provides an accurate and meaningful measure of stem cell number based on the long-term expansion of serial-passaged neurosphere cultures. As this model enables one to detect changes in the prevalence of stem cells in normal and transformed tissues from a variety of organs without the need to phenotypically identify this population, we anticipate this assay will also have a significant impact on the investigation of tissue-specific stem cells throughout the body.

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2. CHARACTERISATION OF ADULT NSCS AND PROGENITOR CELLS

i. Hippocampal Stem Cells

It is now abundantly clear that two regions of the adult mammalian brain continue to benefit from the addition of new neurons throughout the life of an animal: the olfactory bulb and the dentate gyrus of the hippocampus. In the case of the dentate gyrus, neuroblasts generated in the subgranular zone migrate into the adjacent granule cell layer where they begin to differentiate, sending out axonal projections, receiving afferent inputs, and thereby incorporating into the existing circuitry of the region. While adult hippocampal neurogenesis has been demonstrated to occur in all species studied to date, we still know surprisingly little about the nature of the precursor population that produces these neurons and even less about its regulation. What also remains unknown is whether the reservoir of endogenous stem cells that provides for hippocampal neurogenesis resides within the hippocampus or is constantly repopulated by the progeny of stem cells in the subventricular region.

We therefore employed the neurosphere assay and the recently developed neural colony forming cell assay to determine whether a *bona fide* NSC is present in the hippocampal formation. In contrast to the ventricular region directly adjacent to the hippocampus where NSCs are readily detected (red region, Figure 1), we did not find evidence of a stem cell within the hippocampal formation. Rather, dividing cells within the hippocampus exhibit limited proliferation and cannot self-renew, suggesting the presence of a restricted progenitor cell, which occurs at a frequency of about 1 in 9000 (Figure 2). Therefore we conclude that the stem cell underpinning adult hippocampal neurogenesis resides outside the hippocampus, where it generates progenitor cells which migrate into the neurogenic zones and proliferate to produce new neurons and glia.

ii. Periventricular Stem Cells

Surface antigen-based purification

We previously reported the identification and subsequent purification of an essentially pure population of neural stem cells from the adult mouse brain based on its repertoire of cell surface antigens and employing the neurosphere assay as a readout of stem cell activity (Rietze *et al.*, 2001). This represented an essential first step towards our goal of understanding stem cell regulation, as these cells represent an extremely rare (< 0.01%) population of cells in the adult brain. We have since discovered that only a minority (~3%) of neurospheres are stem cell derived, with the majority resulting from more restricted progenitor cells (Reynolds and Rietze, 2005). We subsequently re-evaluated our neurosphere-based purification strategy employing the novel Neural-Colony Forming Cell Assay (N-CFCA), which has the ability to discriminate between stem and progenitor cells based on their proliferative potential, and was developed in the lab as part of a collaborative effort with StemCell Technologies (Vancouver, Canada). Dr Natalie Bull, a post-doctoral fellow in the lab, employed the N-CFCA to successfully demonstrate the absence of stem cells in the adult hippocampus, attesting to the robust nature and acceptance of this assay by the field. By using the N-CFCA as a read-out of stem cell activity, we discovered that while a significant enrichment of stem cells was accomplished by collecting the $PNA^{lo}HSA^{lo}$ population, only 15% of the sphere-forming cells were stem cells.

Therefore, the major focus of the lab remains to determine the phenotype, and thus generate essentially pure populations of neural stem and progenitor cells to enable an unambiguous investigation of these cells. Of interest, we have also developed a mathematical model that can detect changes in the number of stem cells

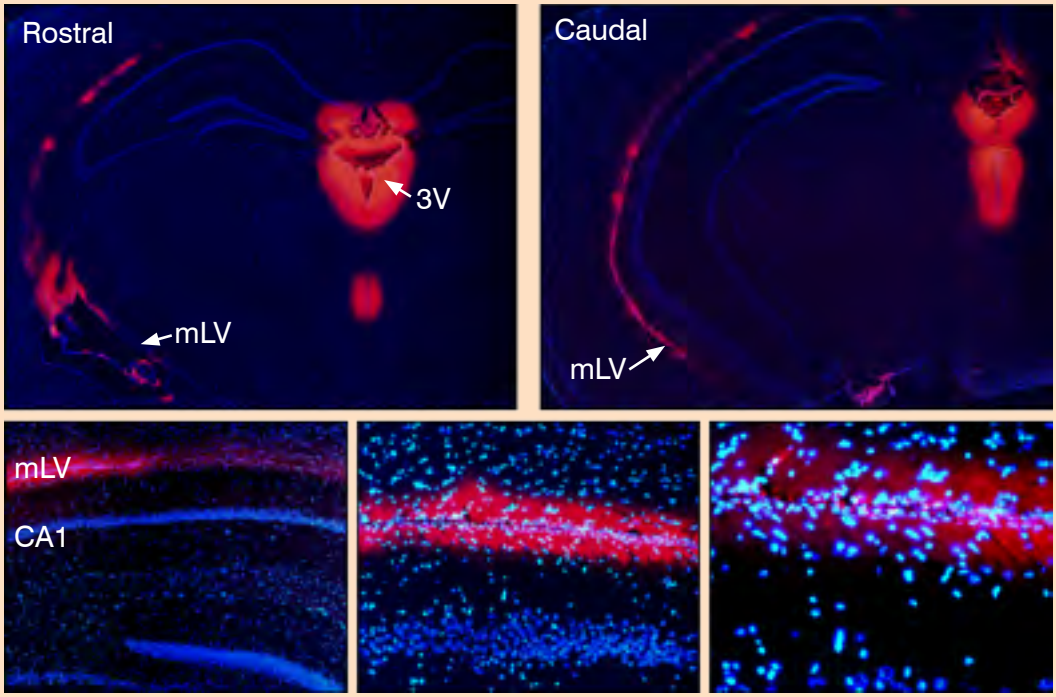


Figure 1: Injections of the lipophilic dye, DiI (shown in red) directly into the lumen of the ventricle were employed to ensure that tissue from the lateral (mLV) and third ventricles (3V) – regions known to contain NSCs – did not contaminate hippocampal cultures.

without the need to phenotypically identify this population, providing the means to discover molecules that specifically modulate stem cell activity. As described in more detail below, growth hormone represents such a molecule.

Functional purification

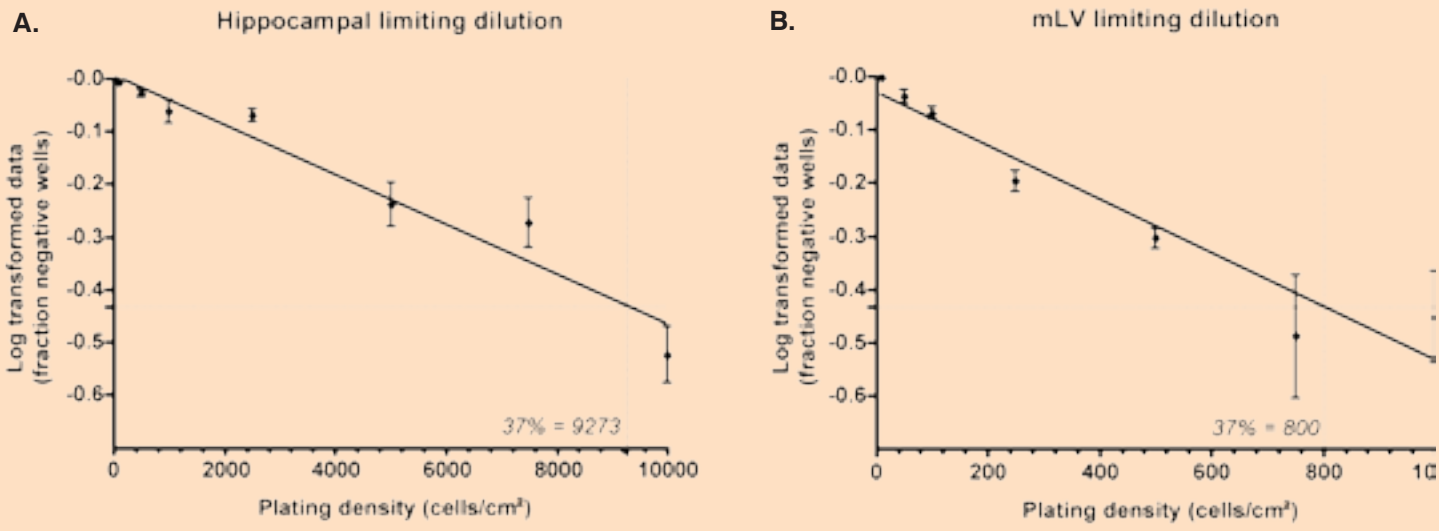
A defining characteristic that is thought to distinguish endogenous neural stem cells (NSCs) from more committed progenitors is their relatively quiescent nature. As a proof of principle, we attempted to identify infrequently cycling endogenous NSCs by "pulsing" dividing cells with bromodeoxyuridine (BrdU) every two hours for 48 hours, or 3 times/day for 1 month. This was followed by "chasing" these cells for up to one year post-injection, over which time rapidly cycling cells will have diluted their label, leaving only slow-cycling or label-retaining cells (LRCs). An analysis of the distribution of LRCs was undertaken by serially sectioning the entire ventricular neuraxis of the adult mouse brain, then counting the number of BrdU-immunoreactive cells that did not colocalise with markers of mature cell types (NeuN, GFAP, O4). This analysis revealed three distinct regions where high concentrations of LRCs were localised. Of interest, these pockets of LRCs correlated exactly with peaks in the number of neurosphere-forming cells that could be harvested. However, as neurosphere formation is indicative of both stem and progenitor cells, we employed the N-CFCA, to distinguish stem from progenitor cells based on colony size, and to determine what percentage of LRCs were indeed NSCs. While NSCs (large colonies) colocalised with pockets of LRCs, the absolute number of large colonies was drastically reduced in comparison to LRC numbers. Thus, while LRCs colocalise spatially with NSCs, this technique cannot be used to exclusively identify NSCs in the adult brain.

3. Activation of endogenous NSCs

The prior detection of growth hormone (GH) and its cognate receptor (GHR) in germinal regions of the developing and adult brain prompted us to investigate whether GHR is expressed on endogenous NSCs, and whether its activation modulates stem cell activity. Accordingly, GHR+ve cells were harvested from the ganglionic eminences of embryonic day 14 (E14) mice, and adult periventricular region, which are known to contain NSCs. These cells were sorted, then plated at clonal density under conditions known to generate neurospheres. While < 1% of the viable cells were GHR+ve, a portion of this population exhibited the cardinal stem cell properties of proliferation, extensive self-renewal, and generation of a large number of progeny, thereby demonstrating the presence of GHR on a population of NSCs in the developing and adult brain. However, the majority of sphere-forming cells were found in the GHR-low population, precluding this antigen as a selective NSC marker.

We next investigated the role that GH plays on NSCs by a) exposing serially passaged cells to GH, b) infusing GH directly into the ventricles of adult mice, and c) culturing adult SVZ stem cells derived from GHR-/- animals. Data analysis using the N-CFCA and mathematical modelling revealed that GHR plays a role in symmetric stem cell divisions as evidenced by an increase in the number of stem cells with the *in vitro* addition of GH and a reduction in their numbers in the GHR-/- animals. Consistent with these results, we found that the direct infusion of GH into the lateral ventricles for seven days resulted in a significant and sustained (up to 120 days post-infusion) increase in the number of endogenous NSCs. Given that the absolute numbers of NSCs are thought to decline with age, stimulation of such cells via GH or its receptor may represent a novel means by which to reverse or prevent the deleterious effects of ageing.

▼ **Figure 2:** Frequency of hippocampal (A) and ventricular (B) sphere-forming cells.



"Our main focus has been how the p75 death signal is controlled by environmental factors, specifically synaptic activity and ion flux ..."
– **Dr Elizabeth Coulson**

COULSON LABORATORY

Unlike cells in most tissues, the vast majority of the neurons present in our brains as young children survive until old age. Undesirable neuronal death occurs in a wide range of neurodegenerative conditions, including motor neuron disease and Alzheimer's disease. Surprisingly, this cell death mimics a cell suicide program which occurs in neurons both during embryonic development and in limited areas of the adult brain, where neurons that are not appropriately connected to other neurons are removed by cell suicide. This death is crucial for constructing and maintaining an optimally functioning brain. As well as underlying neurodegeration, misregulation of neuronal survival may also be the cause of mental illnesses such as depression and schizophrenia.

We are investigating the reasons and ways neurons survive or commit suicide. Our research focuses on a cellular protein, the p75 neurotrophin receptor, which acts as a rheostat, instructing nerve cells either to live or to die. We are researching the molecular mechanisms by which p75 mediates these instructions in cultured developing neurons, in newly born cells of the adult mouse hippocampus and in mouse models of neurodegeneration. Our results are helping us to understand disease processes and have identified candidate treatment strategies for neurodegenerative and neurological conditions.

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BSc (Hons), PhD

Alex Sykes, *BApp Sci (Hons)*

Areechun Sotthibindhu, *BSc (Hons)*

Briony Fox, *BVSc (Hons)*

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Linda May, *BA (Hons), BSc (Hons)*

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Our main focus has been how the p75 death signal is controlled by environmental factors, specifically synaptic activity and ion flux, and by ligand-dependent and -independent cleavage of p75.

We have found that cleavage of p75 regulates its ability to activate death signals and that the cleavage process is dependent on the location of p75 within cholesterol-rich microdomains. However, if fragments of p75 accumulate in these microdomains, death signalling is promoted. Since activity of the p75 cleavage enzymes and cholesterol metabolism are often significantly changed in neurodegenerative conditions, this discovery highlights a mechanism by which the diseased cellular environment may upset the fine balance of

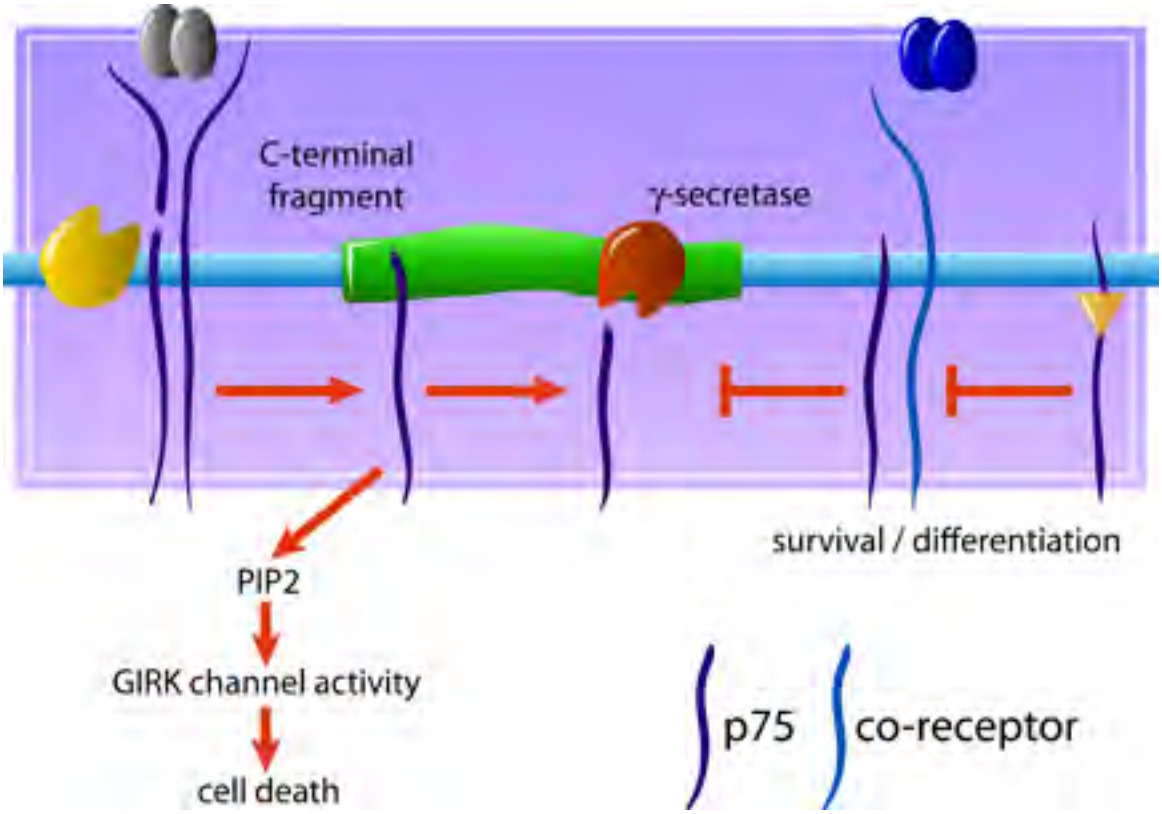
▼ **Coulson Lab: (L–R)** Clare Underwood, Linda May, Michael Colditz, Areechun Sotthibindhu, Alex Sykes, Noura Al-Menhali, Elizabeth Coulson

p75-mediated death and survival signals, thereby promoting neurodegeneration.

During development, optimal survival is not only regulated by trophic factors that counter p75-mediated death signals but also by synaptic activity. We have found that p75-mediated death signals may require synaptic activity controlling ion channels known as G-protein coupled inwardly rectifying K^+ (GIRK) channels. p75 can open these channels, while blocking the flux of K^+ ions through GIRK channels can prevent cell death. It may be that neuronal death signals can only proceed if the GIRK channels are not being used to regulate synaptic activity, thereby ensuring that appropriately connected neurons remain alive.

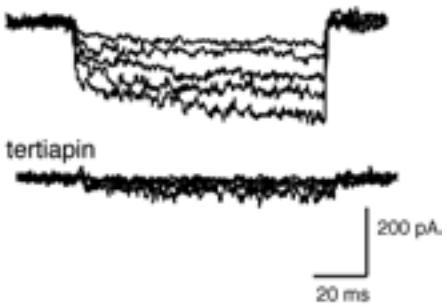
Although p75 is well characterised as a death receptor, the death signalling pathway it activates is not as well defined. Recently it was shown that p75 undergoes regulated membrane proteolysis (RIP) through extracellular metalloprotease- and intracellular γ-secretase-dependent cleavage (Fig. 1 below). We have demonstrated that intracellular p75 cleavage is dependent on extracellular cleavage to produce a C-terminal fragment, which must then move into cholesterol-rich lipid raft microdomains of the plasma membrane — where the γ-secretase resides — to be intracellularly processed.

▼ **Figure 1:** The p75 death signalling is activated by ligand (grey) binding followed by proteolytic cleavage (yellow), generating a c-terminal fragment. Cleavage by γ-secretase (red) terminates death signalling. The c-terminal fragment only signals death when located on a lipid raft (green). This can be prevented by mutations (yellow traingle) or association with a co-receptor.

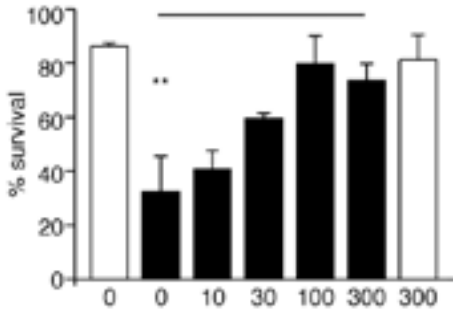


"It may be that neuronal death signals can only proceed if the GIRK channels are not being used to regulate synaptic activity ..."

We have further shown that under conditions where the C-terminal fragment of p75 accumulates in lipid raft domains, cell death of primary neurons is promoted (Fig. 1) whereas cellular factors which prevent p75 death signalling keep this fragment from entering the raft domains. In addition, together with Pankaj Sah we have found that the C-terminal fragment is a novel activator of GIRK channels (Fig. 2). Unlike their traditional activators, p75 activates the GIRK channels independently of G-proteins. Instead, p75 promotes generation of the phosphoinositide second messenger PIP2 (Fig 3), which alone appears sufficient to stimulate GIRK channel activity. We have also found that functional GIRK channels are required for p75-mediated neuronal death (Fig 4). Since, in many neurodegenerative conditions, loss of synaptic input is often coupled with either increased metalloprotease activity or compromised γ-secretase activity which could result in C-terminal fragment accumulation in lipid rafts, our data may explain why p75-mediated neuronal death is most apparent in these circumstances.

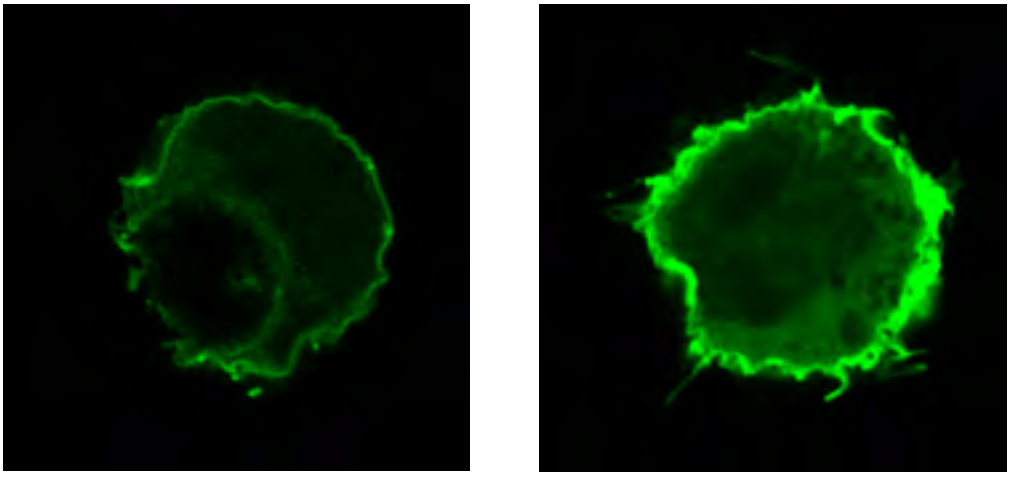


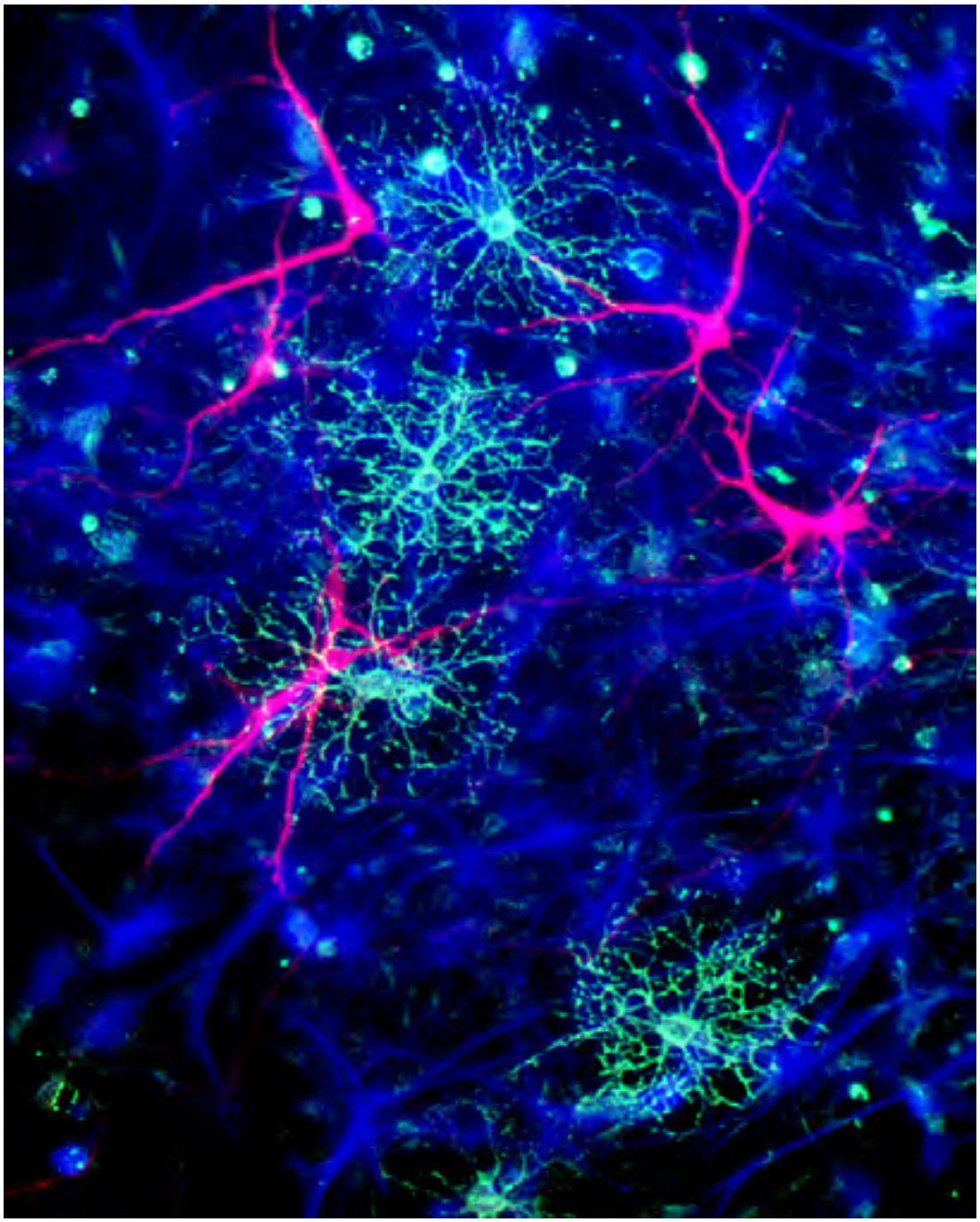
▲ **Figure 2:** Electrophysiological recordings of a cell in which the C-terminal fragment of p75 has shown potassium channel activity. This activity is inhibited by the GIRK channel blocker tertiapin.



▲ **Figure 4:** Assay of neuronal survival of control cells (white bars) and those undergoing p75-mediated cell death (black bars). Neurons treated with the GIRK channel blocker tertiapin are, in a dose-dependent manner, significantly protected from p75-mediated death.

▶ **Figure 3:** Cells in which a green fluorescent protein marker is bound to the phosphoinositide second messenger PIP2. Cells without p75 (left panel) have less PIP2 than cells with p75 (right panel).





▲ Progenitor cells proliferate to form a neurosphere which after differentiation and immunostaining for mature cell types contains neurons (red) and supporting cells including oligodendrocytes (green) and astrocytes (blue).

"Our laboratory is collaborating with paediatric neurologists in the USA to uncover the genes involved in agenesis of the corpus callosum."
– Associate Professor Linda Richards

RICHARDS LABORATORY

QBI's cortical development and axon guidance research investigates how the brain becomes wired up during development. We are interested in understanding how key molecules regulate the migration of neurons within the cortex and the guidance of their axons to their final targets in the brain. Key to understanding this is our model system, the developing corpus callosum.

The corpus callosum is the largest fibre tract in the brain which connects neurons in the right and left cerebral hemispheres.

Malformation of the corpus callosum is associated with more than 50 different human congenital syndromes, although we know very little about how or why these occur. Essential for neurologists in treating children with these disorders is to provide patients and their families with an accurate prognosis. To accomplish this, our laboratory is collaborating with paediatric neurologists in the USA to uncover the genes involved in agenesis of the corpus callosum.

Associate Professor
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BSc (Hons), PhD

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Daphne Kusters, *MSc*
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Grant Mastick, *BSc, PhD*
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Janette Thurley, *BSc*
Michael Piper, *BSc (Hons), PhD*
Nana Sunn, *BSc (Hons)*
Sarah Croft, *BSc (Hons)*
Thomas Fothergill, *BSc (Hons), PhD*
Thomas Pollack
Tianbo Ren, *BSc*

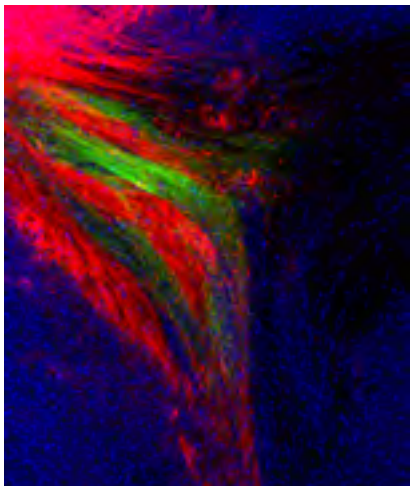
A genetic test would allow doctors to more accurately diagnose and treat patients. This work translates directly from our work in identifying the developmental processes that form the corpus callosum, and the molecular regulation of these events.

One family of molecules we have focused on recently are the Slit and Robo molecules.

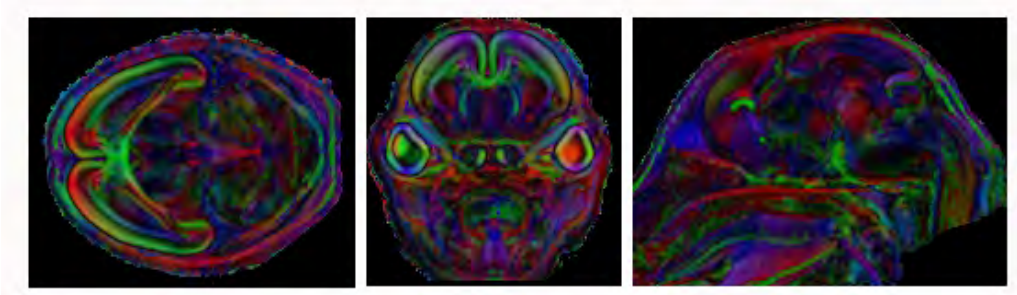
▼ **Richards Lab: (L–R)** Tom Fothergill, Daphne Kusters, Divya Unni, Charlotta Lindwall, Tianbo Ren, Linda Richards

Slit is a chemorepulsive ligand that is essential for guiding callosal axons at the midline. Its receptor, Robo, is also essential. When either of these genes is mutated in mice, defects in callosal formation arise (Figs. 1 and 2). Using both whole-brain imaging (Fig. 3) and histological and molecular techniques, we are uncovering how these genes regulate brain formation. In the coming year, we hope to further understand the role of glial cells in callosal formation and to identify key genes involved in these brain disorders in children.

◀ Figure 1: Immunohistochemistry for GAP 43 demonstrates axonal guidance defects in Robo1 knockout mice (B) compared to controls (A). The arrow indicates aberrant axonal bundles forming at the midline.



▶ Figure 2: Tract tracing analysis using fluorescently labelled dyes showing both the corpus callosum (red axons) and the hippocampal commissure (green axons). In wildtype animals, the corpus callosum and the hippocampal commissure normally remain segregated. In contrast, as shown here, the axons of both commissures co-mingle in large fascicles at the midline in Robo1 knockout mice.



▲ Figure 3: Diffusion tensor magnetic resonance imaging (DTMRI) is a useful technique that displays all the axon tracts within the brain and "colour-codes" their trajectories based on their orientation. Shown is a scan of a wildtype mouse brain in horizontal, coronal and sagittal views (L–R). The green axon tracts are the commissural projections we are interested in studying.

◀ **Richards Lab: (L–R)** Amber-Lee Dawson, Nana Sunn, Grant Mastick, Guy Barry, Michael Piper

"Recently we have identified another important guidance receptor, Ryk, that promotes axon navigation between cortical hemispheres."
– Associate Professor Helen Cooper

COOPER LABORATORY

Cell migration is a fundamental process essential for establishing the architectural plan of the central nervous system during vertebrate embryogenesis. Newly born neurons migrate along predefined pathways to establish the variety of distinct structures present in the adult brain. In addition, newly born neurons must also extend nascent axons to their appropriate targets to establish the extensive network of connections found between neurons in the adult brain.

Research in our laboratory focuses on the netrins and their receptors, neogenin and DCC, a major molecular guidance system driving both axon pathfinding and neural cell migration. Recently we have identified another important guidance receptor, Ryk, that promotes axon navigation between cortical hemispheres.

Associate Professor Helen Cooper
BSc (Hons), PhD

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Clare Seaman, *BSc (Hons)*
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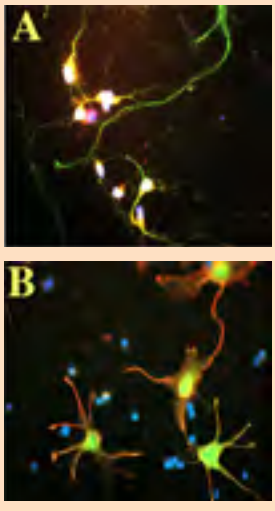
Daniel Fitzgerald, *BS, PhD*
Nigel Kee, *BSc (Hons)*
Stacey Cole, *BBiomedSc*
Tom Keeble, *BSc (Hons)*
Yunyi Wong, *BEng Chem (Hons)*

NEOGENIN AND THE FORMATION OF THE CORTEX

Our studies in the embryonic mouse indicate that neogenin is also important for the formation of the neocortex. We have shown that neogenin protein is present on neurogenic progenitors (i.e. radial glia) (Fig. 1A, green) within the embryonic cortex when neurogenesis is at its peak. Neogenin is also found on interneurons migrating from the ventral telencephalon into the embryonic cortex (Fig. 1B, red). Our future research will investigate how neogenin and its ligands contribute to cortical development in the mammal.

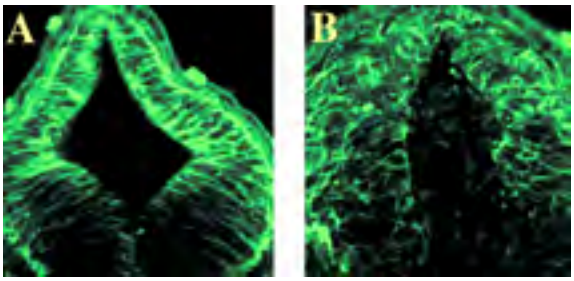


▶ Figure 1: Neogenin is expressed on neural progenitors (A) and migrating newly born interneurons (B) in the early embryonic mouse brain.

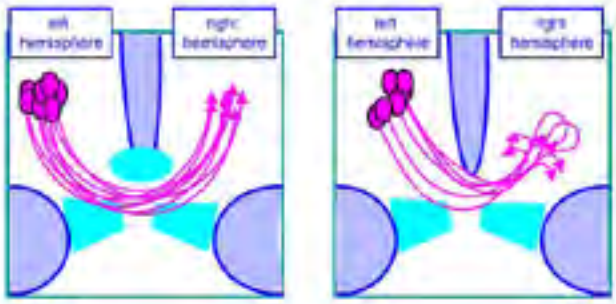
▶ **Cooper Lab: (L–R)** Stacey Cole, Nigel Kee, Yunyi Wong, Helen Cooper (absent: DanaKai Bradford, Tom Keeble)

NEOGENIN AND NEURAL TUBE DEVELOPMENT

Our recent studies have used zebrafish and *Xenopus* (frog) embryos as developmental models to demonstrate that neogenin is a key receptor responsible for the correct formation of the neural tube, the earliest identifiable brain structure. We have shown that loss of neogenin impairs neural migration, resulting in significant morphological abnormalities in the neural tube (Fig. 2A, wildtype neural tube; Fig. 2B, mutant neural tube). Furthermore, these abnormalities eventually suppress neuronal production throughout the developing brain. Similar abnormalities are seen during human neural tube formation leading to anencephaly and spina bifida. Such failures in neural tube closure occur in one in a thousand human pregnancies. Therefore, understanding the role of neogenin in neural tube development is providing new insights into prevalent human developmental abnormalities.



▲ Figure 2: (A) Neuroepithelial cells align in an organised fashion in the wildtype frog neural tube. (B) Loss of neogenin during early brain development disrupts neuroepithelial cell polarity.



▲ Figure 3: (Left panel) As the mammalian brain develops, axons extend from neurons in the cortex and travel via the corpus callosum into the opposite hemisphere. (Right panel) When the Ryk receptor is missing, axons reach the midline but cannot escape into the adjacent hemisphere.

RYK GUIDES AXONS ACROSS THE **CORPUS CALLOSUM**

The corpus callosum is the major interhemispheric commissure in the human brain, comprising about 3 million myelinated fibres which connect one side of the neocortex to the other. In patients with a severed corpus callosum, perceptual interactions between hemispheres do not occur, resulting in the aberrant integration of sensory and motor information.

More than 50 different human congenital syndromes, often associated with mental retardation and epilepsy, have been described in which agenesis of the corpus callosum occurs. In these syndromes cortical axons approach but are unable to cross the midline of the forebrain and instead form disorganised bundles of axons (Probst bundles) on the ipsilateral side (i.e. on the same side as they originate).

Our lab has recently identified a guidance receptor, Ryk, that acts on the contralateral side of the midline (i.e. on the opposite side of the midline from where the axons originate) to promote callosal axon escape from the midline into the adjacent hemisphere. Therefore, Ryk is a new molecule responsible for linking the two hemispheres of the brain.

This project will provide clues as to how major axon tracts are formed during embryogenesis, and suggest novel strategies to encourage axon regrowth and correct pathfinding in the damaged or diseased brain.

"Understanding the mechanisms that underlie these amygdala-related behaviours will ultimately lead to the development of targeted treatments for psychiatric disorders such as anxiety and stress."

– Professor Pankaj Sah

SAH LABORATORY

The mammalian brain is composed of about 10 billion cells, called neurons. These neurons are connected in intricate patterns, with each cell making and receiving nearly 10,000 connections. The number of connections between nerve cells in the brain is therefore immense. It is thought that learning and memory formation in the brain result from changes in the strength of connections between neurons.

Professor Pankaj Sah
BSc, MBBS, PhD

Alan Woodruff, *BSc (Hons), PhD*
Andrew Delaney, *BSc (Hons), PhD*
Esmaili Abolghashem, *BSc (Hons), PhD*
Francois Windels, *BSc,PhD*
Jai Polepalli, *BSc, MSc*
James Crane, *BSc (Hons), PhD*
John Power, *BSc, MSc, PhD*
Nicola Watts, *BPsych (Hons)*
Pavel Prosselkov, *PhD*
Petra Sedlak, *BSc (Hons)*

To understand how the brain can learn and store information, we need to understand the properties of its resident neurons, the properties of their connections and how these change with learning.

Our lab focuses on a part of the brain called the amygdala – a small almond-shaped structure that is involved in processing emotion-related information.

Emotions such as fear, happiness, disgust and hate all activate the amygdala. Disorders of amygdala processing in turn lead to emotion-related illnesses, such as anxiety, panic attacks and post-traumatic stress.

The amygdala is intimately involved in a simple learned behaviour called fear conditioning. This occurs when an emotionally neutral stimulus – such as a tone or a light – is paired with a fear-producing stimulus such as a mild shock.

After a small number of such pairings, the neutral stimulus comes to evoke a fearful response. This response, which is seen in virtually every animal from flies to humans, is

▼ **Sah Lab: (L–R)** John Power, Jai Polepalli, James Crane, Nicola Watts, Pankaj Sah

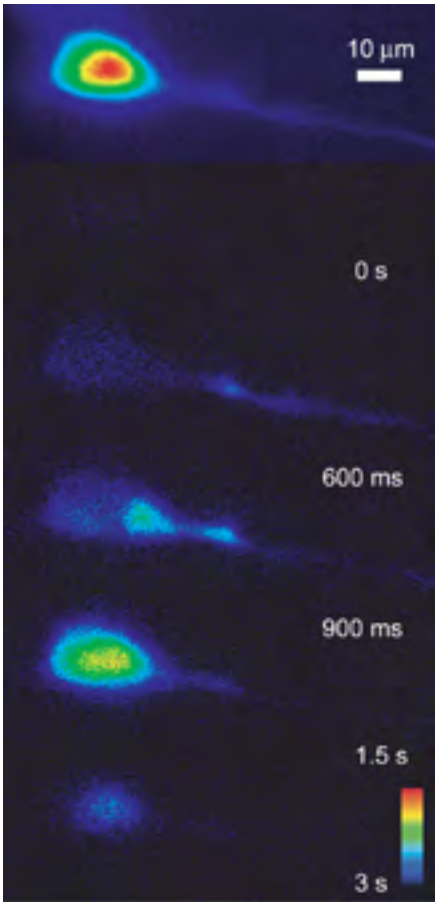
quickly learnt and is remembered for years, requiring the storage of memory.

In humans, post-traumatic stress may be the result of such pairing of stimuli during stressful times, such as accident or war.

Understanding the mechanisms that underlie these amygdala-related behaviours will ultimately lead to the development of targeted treatments for a number of psychiatric disorders.

In our lab, we study the circuitry of the amygdala and how it changes using a range of behavioural, physiological and imaging techniques. These studies are revealing new information on the intrinsic circuitry of the amygdala and the properties of the receptors that are present there.

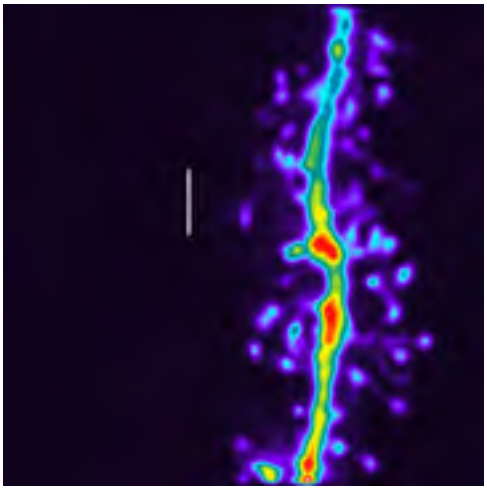
One of our groups is examining the properties of cells in the input side of the amygdala – part of the limbic system that is involved in assigning emotional significance to cognitive events. We have shown that cells within the lateral and basal nuclei can be divided into two broad categories: pyramidal cells and interneurons. Pyramidal cells form the major type of cell (93 per cent) and are similar to excitatory cells found throughout the cortex. The remaining cells are



◀ Rises in calcium in a neuron in the amygdala that has been loaded with a calcium indicator. The top panel shows the images of a cell from which we were recording. The lower panels show the response to synaptic stimulation. Synaptic stimulation evokes a rise in the cytosolic calcium that is shown as a change of colour, with brighter colours indicating larger rises in calcium. The measurements on the right indicate the time after synaptic stimulation.

▼ **Sah Lab: (L–R)** Pavel Prosselkov, Francois Windels, Petra Sedlak, Andrew Delaney, Louise Faber (absent: Alan Woodruff, Esmaili Abolghashem)

"This finding may have therapeutic implications as a potential target for new classes of drugs."

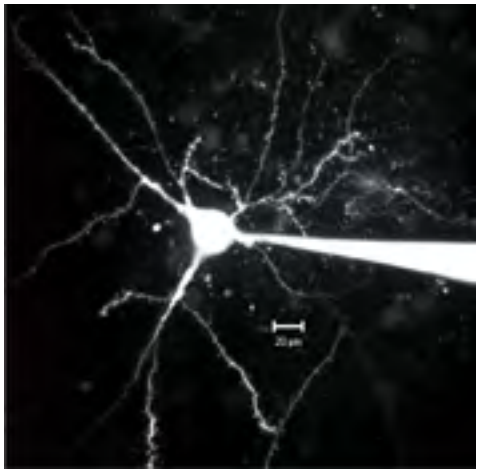


▲ The leaf-like projections coming from the dendrite (spines) are where individual synaptic connections are made. The spines have been coloured for clarity. Scale bar indicates 2 microns.

inhibitory and form extensive connections with the excitatory cells in the amygdala. We were surprised to learn that the properties of synaptic inputs onto interneurons were quite different from those onto pyramidal neurons. These findings indicate that the modulation of inhibitory pathways may be an important control mechanism within the amygdala. The laboratory is now examining the properties of these neurons, using a combination of electrophysiological and imaging techniques.

▶ A neuron in the amygdala that has been loaded with a fluorescent dye and then imaged on a multiphoton imaging system. The recording electrode can be seen attached to the neuron.

Another area of research involves studying the output side of the amygdala – the central nucleus. This structure is divided into two main parts, medial and lateral. It has recently been shown that cells in the lateral division are inhibitory and make local circuits, while cells in the medial division project out of the amygdala. The laboratory has been examining the effects of a class of drugs called benzodiazepines (e.g. diazepam or valium). These are widely used as anxiolytics and their role in the amygdala is of great interest. These drugs are thought to work by potentiating the actions of the major inhibitory transmitter in the brain, gamma amino butyric acid (GABA). The research team has found that the central nucleus also contains a second type of GABA receptor, which is inhibited by benzodiazepines. This finding may have therapeutic implications as a potential target for new classes of drugs.



QBI'S RECENT RESEARCH ACHIEVEMENTS IN **SYNAPTIC PLASTICITY**

1 As in most parts of the brain, two types of neurons are present in the amygdala – excitatory neurons that use glutamate as the transmitter and interneurons that are inhibitory and use GABA as the transmitter. We have been investigating the properties of the connections between excitatory and inhibitory cells in the amygdala. These experiments have shown that among the interneurons that express the marker parvalbumin, four different types of neuron are present. These different types of interneuron can be separated on the basis of their electrophysiological properties and the types of connections they make with excitatory neurons. This is the first description of interneuron connectivity in the amygdala.

2 Among the interneuron population we have identified a previously unknown type of cell. GABAergic interneurons are generally thought to be inhibitory cells that reduce the firing of other cell types in the adult brain. We have found that there is a GABAergic interneuron in the amygdala that can excite projection neurons. This is a strong connection and can drive the projection cells to threshold.

3 The amygdala has extensive innervation by many neuromodulatory transmitters such as dopamine, serotonin and acetylcholine. The activity of these transmitters is well known to have modulatory actions on learning and memory formation. However, how they produce these effects is not known. We have shown that activation of metabotropic glutamate and acetylcholine receptors on excitatory neurons in the amygdala can cause the release of calcium in the dendrites that propagates as a wave and invades the nucleus in these cells. These experiments reveal a novel role of these transmitters in controlling nuclear calcium and perhaps controlling gene transcription.

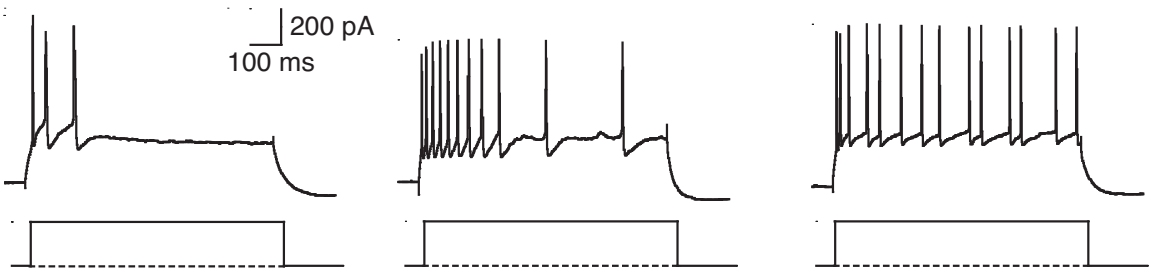
4 At glutamatergic synapses, released glutamate activates two main types of receptors: AMPA receptors that mediate fast transmission and NMDA receptors that allow calcium influx and are required for the induction of synaptic plasticity. We have now found that calcium influx via NMDA receptors also activates a calcium-dependent potassium channel in the postsynaptic membrane. These channels are SK channels and blockade of SK channels can enhance synaptic plasticity at these synapses. SK channels have been known for many years to be responsible for controlling cell-firing properties. Our results show a novel role of these channels in synaptic transmission.

FABER LABORATORY

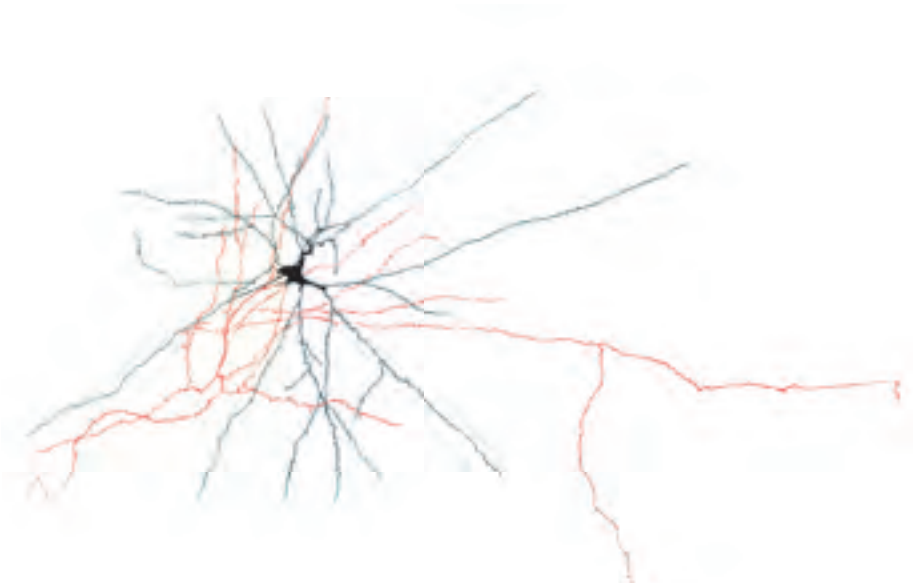
Dr Louise Faber
BSc (Hons), PhD

Part of our work has focused on the cellular physiology of the lateral amygdala, the region in the amygdala that receives polymodal sensory input from cortical and subcortical structures. It is here that the cellular processes underlying the formation and storage of emotional memories, such as those that are laid down during fear conditioning, are thought to occur. We have investigated the physiological properties of pyramidal neurons, the excitatory glutamatergic cells that make up the majority of neurons in the lateral amygdala. We have characterised the action potential discharge properties of pyramidal neurons in the lateral amygdala, and found that these neurons show varying degrees of spike frequency adaptation, the ability to stop or slow firing while the cell is still depolarised (Fig. 1). We have correlated these intrinsic firing properties with the morphological properties of these neurons (Fig. 2). We have also identified and characterised the voltage- and calcium-dependent potassium conductances that determine the firing patterns of pyramidal neurons, in addition to how these conductances are modulated by neurotransmitters, such as noradrenaline, acetylcholine and 5HT. During the past few years, our work has focused on synaptic transmission and plasticity in the lateral amygdala. We have demonstrated that a non-selective cation channel, the transient receptor potential (TRP) channel, is activated synaptically following activation of metabotropic glutamate receptors. We have also discovered a novel role for small conductance calcium-activated potassium (SK) channels in limiting synaptic transmission and plasticity in the lateral amygdala through shunting of excitatory postsynaptic potentials (Fig. 3). In coming years, we will further characterise the role of SK channels in controlling the excitability of the lateral amygdala.

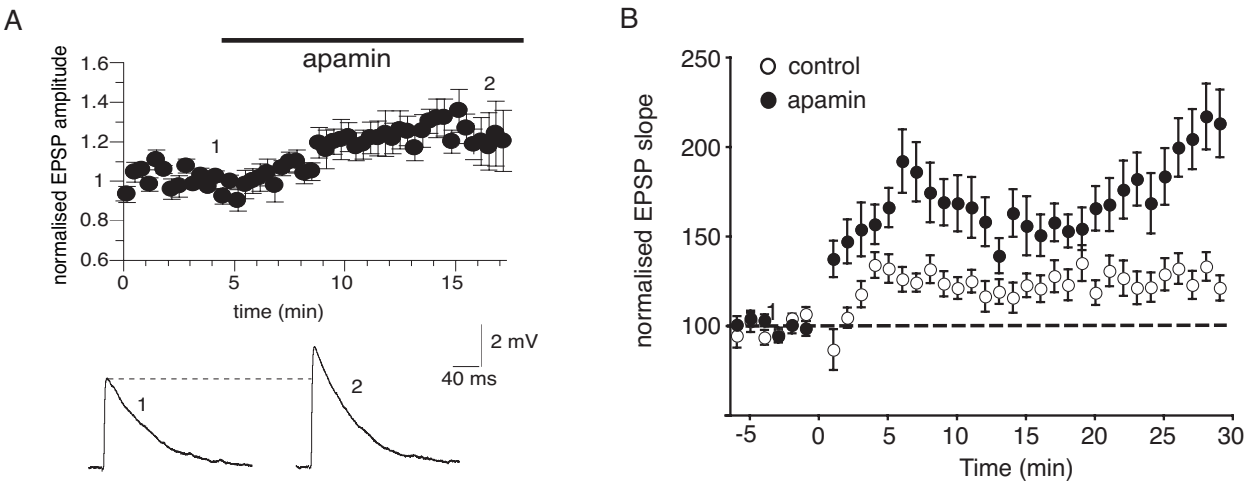
▲ NHMRC RD Wright Fellow, Dr Louise Faber, who is investigating the physiological properties of pyramidal neurons, which are excitatory glutamatergic cells and make up the majority (~90%) of neurons in the lateral amygdala.



▲ Figure 1: Pyramidal neurons in the lateral amygdala display a continuum of firing properties in response to a depolarising current injection (lower traces). These range from cells that show complete spike frequency adaptation and stop firing in response to depolarisation (left trace) to cells that fire repetitively with depolarisation (right trace).



▲ Figure 2: Camera lucida reconstruction of a lateral amygdala pyramidal neuron. The axon is shown in red.



▲ Figure 3: SK channels shunt excitatory synaptic transmission and plasticity in the lateral amygdala. (A) Application of the selective SK channel blocker apamin enhances the excitatory postsynaptic potential (EPSP). The horizontal bar shows when apamin was applied. EPSPs at time points in the graph are shown in the lower traces. (B) Apamin enhances long-term potentiation compared to control following tetanisation of cortical afferents to lateral amygdala pyramidal neurons.

"Currently the lab is investigating a theory of optimal gradient detection based on Bayesian statistical concepts, and how axonal sensitivity to gradients can be modulated."

– Associate Professor Geoffrey Goodhill

GOODHILL LABORATORY

Computational neuroscience at QBI is focused on understanding the computational rules by which the brain develops; in particular, how stem cells form, how neurons become wired together, and how initial patterns of wiring are refined by specific patterns of neural activity.

Using a novel experimental assay, Associate Professor Geoffrey Goodhill's laboratory has, for the first time, mapped the response of axons to molecular gradients of different steepnesses and absolute concentrations. Remarkably, this showed that neuronal growth cones can detect concentration differences as small as one molecule across their spatial extent, making them the most sensitive gradient detection devices yet known.

In related computational work, the lab has shown that a mechanism by which growth cones could achieve this astonishing sensitivity in the face of inevitable stochastic fluctuations in receptor binding is to average receptor binding measurements across both space and time. Currently the lab is investigating a theory of optimal gradient detection based on Bayesian statistical concepts, and how axonal sensitivity to gradients can be modulated.

The lab has also made considerable progress in understanding the computational principles underlying map formation in the visual system. Using a highly successful model of visual map development, they have shown that the elegant geometrical relationships observed experimentally between visual feature maps emerge naturally as a consequence of coverage and

Associate Professor Geoffrey Goodhill
BSc (Hons), MSc, PhD

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Duncan Mortimer, *BSc (Hons)*
Guy Barry, *BSc, PhD*
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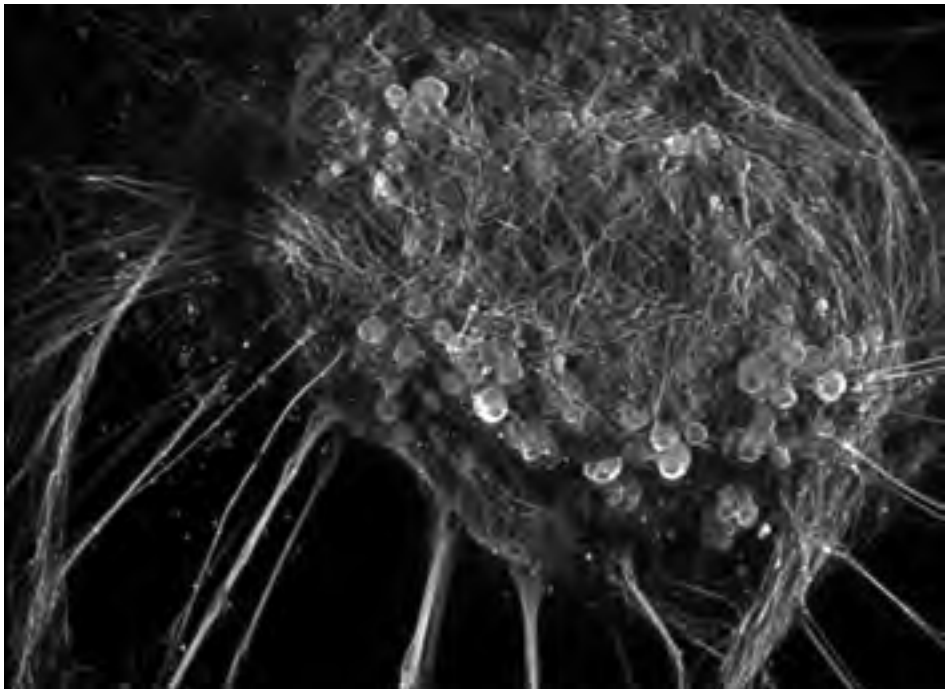
William Rosoff, *BA, PhD*
Zac Pujic, *BSc (Hons), PhD*

▼ **Goodhill Lab: (L – R)** William Rosoff, Duncan Mortimer, Zac Pujic, Clare Giacomantonio, Guy Barry, Geoffrey Goodhill (absent: Huajin Tang)



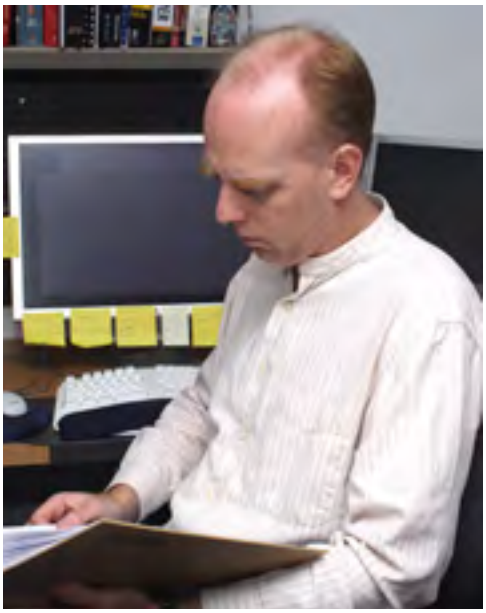
▲ Rat dorsal root ganglion cell explant grown for two days in a 3D collagen gel.

continuity constraints. Furthermore, this model naturally captures the changes in these relationships that occur with various types of visual deprivation. One particular study has investigated the role that angioscotomas (shadows cast by retinal blood vessels) may play in the organisation of visual cortical maps. Besides accounting for the important experimental results, this work offers an unexpected explanation for why angioscotoma representations have so far been seen in only one species of monkey.

▶ Simulation illustrating the competition for control of ocular dominance column structure between cortical shape and the representation of an angioscotoma (shown in red).

Currently the methodology employed by the neurosphere assay includes the manual counting and sizing of neurospheres, which preclude high-throughput experimentation.

ERICKSSON LABORATORY



▲ Dr Geoffery Ericksson, a computational neuroscientist at QBI whose wide ranging research interests include programming, statistics, algorithms, assays, filters and flow cytometry.

NEUROSPHERE ASSAY PROJECTS

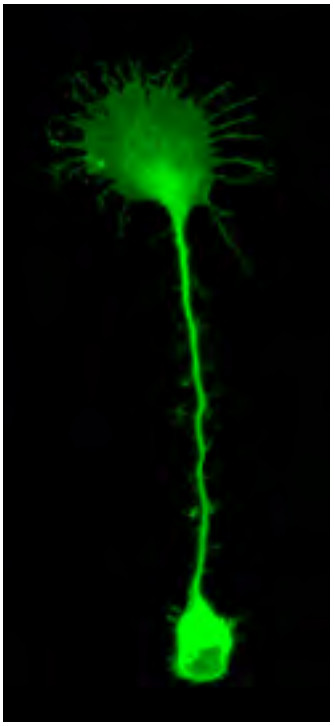
The Neurosphere Assay (NSA) has gained general acceptance as an appropriate method to isolate, expand and calculate stem cell frequency. We have recently shown that the NSA, as presently used, is not an accurate or meaningful predictor of stem cell numbers. To rectify this situation a team of scientists (including Geoffery Ericksson, Brent Reynolds, Rod Rietze and Kristin Hatherley from QBI, as well as Kevin Burrage and Pamela Burrage from the Advanced Computational Modelling Centre) has constructed a mathematical model based on the assumption that during serial passage a stem cell will proliferate longer than a non-stem cell. The model shows that the relative frequency of long-term proliferating cells (aka stem cells) can be calculated by averaging the relative expansion of each passage. Once the relative frequency is known, it is then possible to calculate the effective stem cell symmetric division rate.

Currently the methodology employed by the NSA includes the manual counting and sizing of neurospheres, which precludes high-throughput experimentation. We have devised an automated approach to the counting and sizing problem by using simple image-processing techniques. This automated approach has been validated against manually counted results. The use of this program will relieve researchers from a labour-intensive task, thereby increasing productivity. The increase in throughput afforded by this approach will allow new experimental approaches which have not previously been undertaken due to the high-data volumes.

FLOW CYTOMETRY PROJECTS

The ability to parse flow cytometry standard (FCS 3.0) files directly gives scientists the opportunity to evaluate their flow cytometry data in novel ways. Working closely with QBI's Director of Flow Cytometry Geoff Osborne, Dr Geoffery Ericksson has written and made available to the scientific community a FCS parser which is the only freely available library with C++ bindings. The library was written in the STL style and maintains runtime efficiency by using 'policies' (Alexandrescu 2001) at compile time.

Using the above parser we have invented and implemented a new method of sorting in flow cytometry that is based on the



▲ Rat dorsal root ganglion cell extending a neurite tipped with a growth cone on a two-dimensional substrate

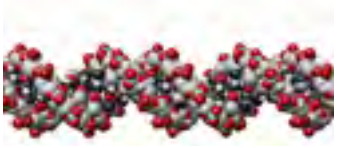
frequency of occurrence of measured values in multidimensional space. This method is ideally suited to samples where the flow cytometric phenotype is poorly known or uncharacterised, yet the frequency of a particular subpopulation is known. It is thus applicable in tasks as diverse as sample decontamination to rare, or unique, event sorting, or conversely every combination of event sorting.

DISCRIMINATIVE BILATERAL FILTER

Image filtering is an important aspect of scientific image processing with the goal of increasing signal-to-noise ratios. Together with the Hankamer lab at UQ's Institute for Molecular Bioscience, QBI's Dr Geoffery Ericksson has devised a new image-processing tool – the discriminative bilateral (DBL) filter – which is based upon the bilateral filter implementation of Jiang *et al.* (2003). In contrast to the latter, the DBL filter can distinguish between object edges and high-frequency noise pixels through the use of an additional photometric exclusion function. As a result, high frequency noise pixels are smoothed, yet object edge detail is preserved. To date the DBL filter has been shown to be effective in reducing noise in electron microscopy micrographs.

SWARMPS SOFTWARE

SwarmPS is a feature-rich GUI-based software package to manage large scale, semi-automated particle picking projects. The software, developed in collaboration with the Hankamer lab at UQ's Institute for Molecular Bioscience, provides cross-correlation and edge-detection algorithms. Algorithm-specific parameters are transparently and automatically determined through user interaction with the image, rather than by trial and error. Other features include multiple image handling (~100), local and global particle selection options, interactive image freezing, automatic particle centring, and full manual override to correct false positives and negatives. SwarmPS is user-friendly, flexible, extensible, fast and capable of exporting boxed-out projection images, or particle coordinates, compatible with downstream image-processing suites.



WALLACE LABORATORY

Dr Robyn Wallace
BSc (Hons), PhD

Tim Butler, BSc (Hons)

"Mouse models provide an excellent opportunity to study the genetic and molecular mechanisms associated with MND."
– Dr Robyn Wallace

The Neurogenetics Laboratory is focused on elucidating molecular mechanisms of diseases of the central nervous system. We are focusing on two disorders that are associated with nerve cell degeneration; epilepsy and motor neuron disease.

Epilepsy is a common, complex disorder with a strong genetic component. We have successfully identified several human epilepsy genes and are continuing to characterise the functional consequences of the mutations.

Three families displaying autosomal recessive inheritance of epilepsy have been mapped to specific chromosomal regions (Fig. 1). We are now screening candidate genes from these regions in an attempt to identify the underlying disease-causing mutations.

Sodium channel mutations are associated with a wide variety of epilepsy syndromes. We are examining the functional consequences of different sodium channel mutations *in vitro* (Fig. 2). Based on the results of the *in vitro* experiments, one mutation will be selected to create a mouse model of epilepsy for *in vivo* analyses.

UNDERSTANDING MND

Motor neuron disease (MND) is a rare disorder characterised by progressive loss of nerve cells in the brain and spinal cord. MND is generally fatal within one to five years of onset and there is currently no effective treatment. This is largely due to the lack of understanding of the mechanisms involved.

Mouse models provide an excellent opportunity to study the genetic and molecular mechanisms associated with MND. However very few mouse models currently exist that are relevant to the disease. Identifying further models will lead to the identification of novel genes and may indicate new pathways associated with MND.

Through the Australian Phenomics Facility we have access to hundreds of mice carrying thousands of random-point mutations. We are screening these mice for loss of motor function in an attempt to identify genes relevant to MND. Four mice have already been identified that warrant additional characterisation (Fig. 3).

About 10 per cent of patients have a family history of MND. A new collaboration with Zhengzhou University in China has been established to collect data from families with inherited forms of MND. This will facilitate linkage mapping and identification of the genes involved.

A small proportion of MND patients carry mutations in the superoxide dismutase (SOD1) gene. We are also investigating ways of preventing the cell death associated with MND in SOD1 transgenic mice.

▼ Tim Butler and Ross Maclean
Research Fellow, Dr Robyn Wallace

In their search for genetic markers for motor neuron disease, QBI's Neurogenetics Laboratory is studying mice that have been bred with random genetic mutations. The mice are given a grip-test that provides researchers with a measurement of muscle strength, a factor which might indicate genes associated with motor neuron disease.

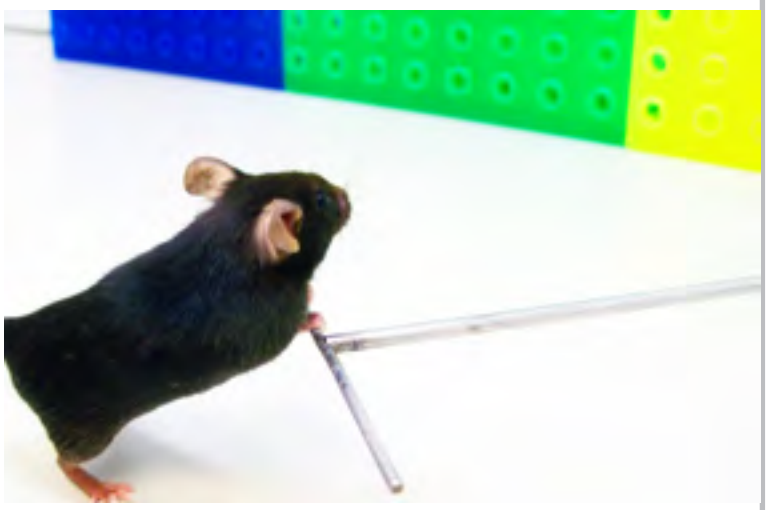
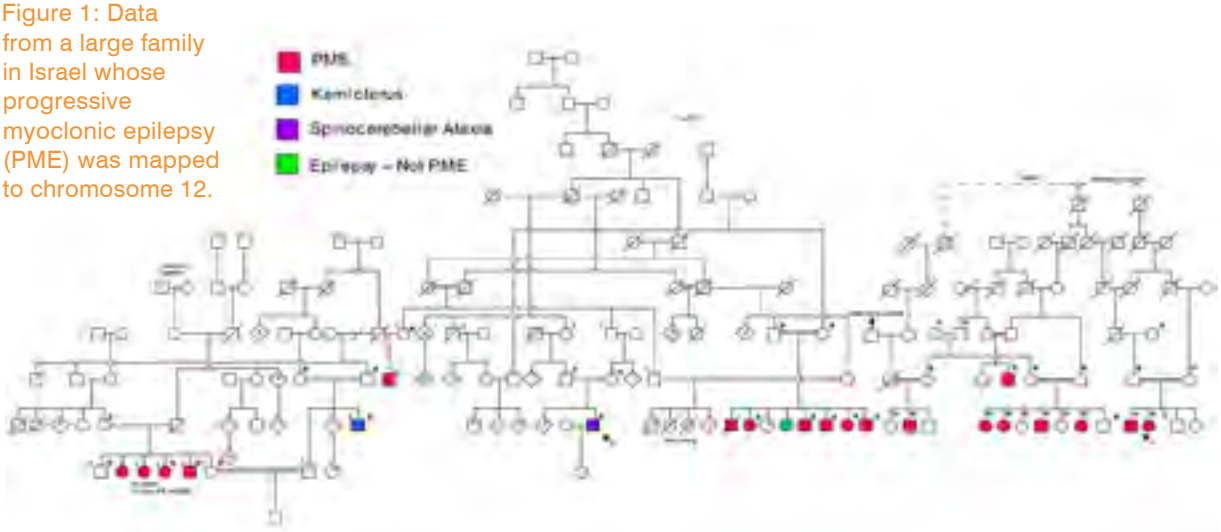


Figure 1: Data from a large family in Israel whose progressive myoclonic epilepsy (PME) was mapped to chromosome 12.



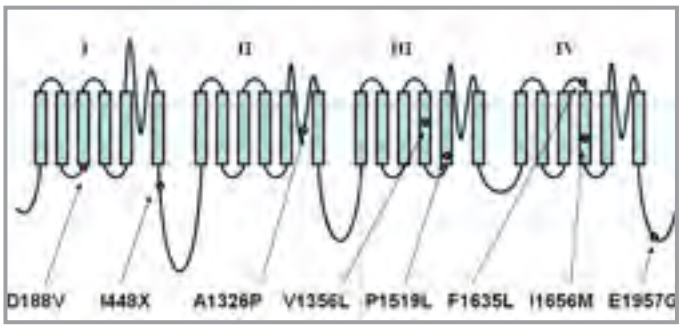


Figure 2: Schematic representation of a sodium channel, showing the location of the epilepsy-associated mutations selected for detailed electrophysiological analysis.

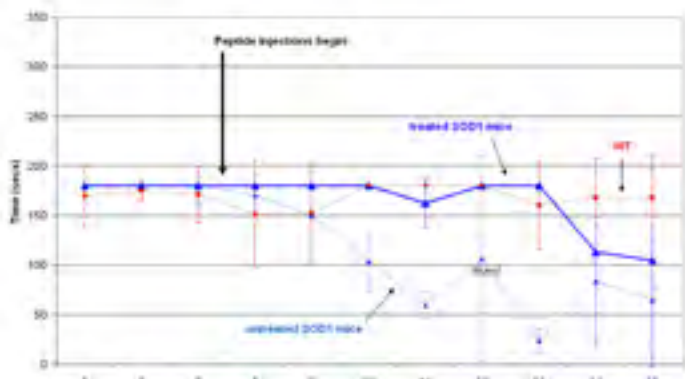


Figure 3: A graph showing the length of time mice were able to keep walking on a rotating rod. Performance improved in SOD1 mice following treatment with a peptide designed to block neurotrophin-dependent cell death.

"Over recent decades, biomedical scientists have forged a balanced appreciation of the strengths and weaknesses of 'animal models' of human disease." **– Professor John McGrath**

McGRATH LABORATORY

John McGrath
MBBS, MD, PhD, FRANZCP

Darryl Eyles *BSc, Grad Dip (Clinical Biochemistry), PhD*
James Kesby, *BSc (Hons)*
Lauren Harms, *BSc (Hons)*
Louse Harvey, *BSc (Hons)*
Pauline Ko, *BBiotech (Hons)*
Thomas Burne, *BRurSc (Hons), PhD*
Xiaoying Cui, *MBBS, PhD*

SCHIZOPHRENIA is a poorly understood group of brain disorders that impacts on higher cognitive functions. Evidence suggests that schizophrenia is associated with altered early brain development (i.e. prenatal or early life).

Both genetic and non-genetic factors increase susceptibility to schizophrenia. This makes the study of developmental neurobiology important for schizophrenia research. The Queensland Centre for Mental Health Research (QCMHR), an affiliate of the Queensland Brain Institute, examines how various risk factors associated with schizophrenia can disrupt brain development.

QCMHR is focusing on two environmental risk factors for schizophrenia based on strong epidemiological support, namely low prenatal vitamin D and advanced paternal age. Changes in either nutrition or gene integrity may alter the orderly cascade of brain development.

Over recent decades, biomedical scientists have forged a balanced appreciation of the strengths and weaknesses of 'animal models' of human disease. In particular, those interested in the pathogenesis of neuropsychiatric disorders such as schizophrenia have matured beyond the naïve belief that any one animal model could ever mimic the broad phenotype of this imperfectly understood group of disorders. In its place, various complementary animal models have been developed that address different but overlapping research questions.

For example, animal models can (a) explore the role of candidate genes in brain development via transgenic animals, and (b) examine the immediate and long-term consequences of environmental exposures

Artwork: Craig Finn 'Schizophrenia'

associated with neuropsychiatric disorders, such as advanced paternal age, prenatal infection, hypoxia or low levels of vitamin D.

While clinical research is important, animal models remain the only practical tool that will allow us to unravel the mechanisms of action linking early life disruptions and later adult neuropsychiatric disorders.

QCMHR has demonstrated that an early life nutritional exposure (low developmental vitamin D) can alter the trajectory of brain development in the rat. Furthermore, the exposure results in an adult behavioural phenotype highly suggestive of altered dopaminergic and/or glutaminergic signalling. These pathways are strongly implicated in the pathogenesis of schizophrenia. QCMHR believes that this developmental research will help reveal vulnerable pathways implicated in schizophrenia.

QBI has recently installed a new-generation instrument that combines the visual power of microscopy and the statistical rigour of flow cytometry in a single bench-top platform.

NEUROIMAGING AND ADVANCED TECHNOLOGIES

To date, the neurosciences are one area of scientific endeavour in which flow cytometric techniques have had little impact. However, recent technological improvements in this field have opened up new avenues for research.

At QBI, we have made a concerted effort to establish the first flow cytometry facility in the world that is dedicated to neuroscience. During the initial phase, these efforts have involved specifically tailoring the techniques and technology to suit neural cells – particularly neural stem cell identification and separation. Subsequent work will build on this foundation by applying laboratory automation to such diverse problems as glioma phenotyping and rare event enumeration of neural stem cells and enrichment of these populations of cells.

The cell sorter has become a cornerstone technology for the study of haematopoietic stem cell function, and indeed for the study of haematopoiesis in general. This is due not only to its ability to reliably sort specific populations of stem, progenitor, and more differentiated blood cell types, but also because it can provide quantitative information pertaining to the viability, DNA content, mitotic activity, and protein expression patterns of specific cell types.

In light of recent advances that allow the sorting of essentially pure populations of viable neural stem cells, neural crest cells, and post-mitotic neurons using flow cytometry, we have established a world-class facility for the sorting of neural tissue.

At the heart of the QBI Flow Cytometry Facility is a range of state-of-the-art cell sorting flow cytometers. The flagship of these instruments is the Cytopeia Influx, the world's first commercially released five-laser capable high-speed cell sorter. This instrument offers unparalleled flexibility to excite a wide range of fluorochromes and is coupled to an automated sample delivery system which allows cultured neural cells from multiwell plates to be injected, selected and cloned into specific collection vessels for further studies.

The products of this process allow us to undertake functional cell-based assays on particular cells, the characteristics of which we have quantified, so that, for example, we can screen compound libraries for compounds that affect selected brain tumour cells, but do not affect normal cells. Along with specific cell sorting, we apply detailed analyses of cell populations using high-throughput screening techniques to identify rare cell types and sub-types of cell populations.

◀ **Flow Cytometry Team (L–R)**: Virginia Nink, Damien Gardiner, Geoff Osborne.

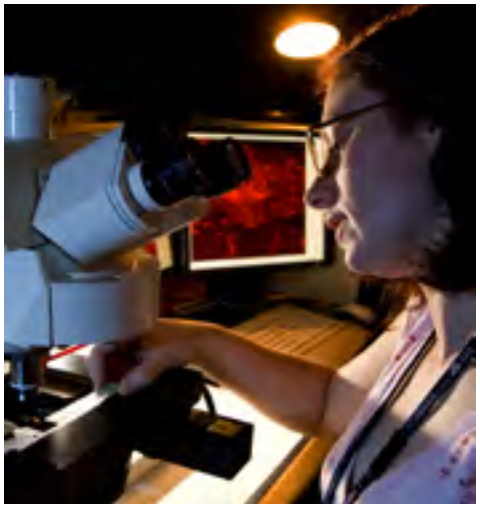
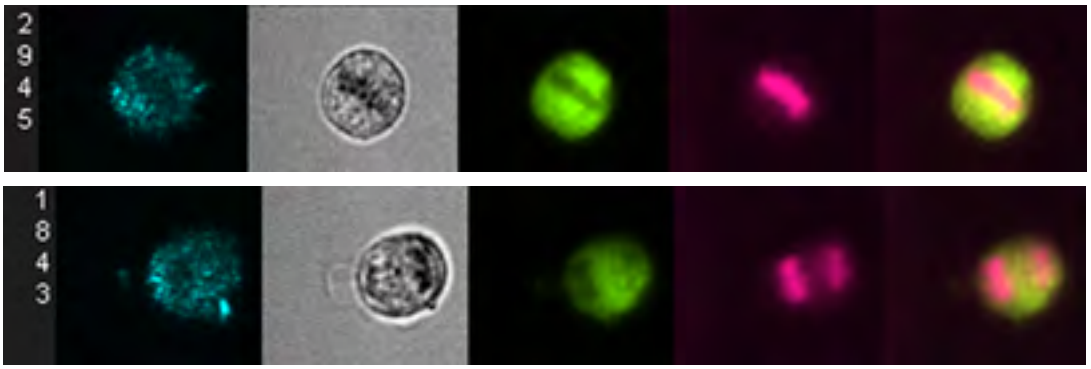


Photo: Chris Stacey, UQ

▲ Confocal microscopy is a vital tool in the study of the molecular interactions that are occurring in the brain – Research Assistant, Fiona Rogers.

IMAGESTREAM SYSTEM
PROVIDES 'HIGH CONTENT' IMAGING

QBI has recently installed a new-generation instrument that combines the visual power of microscopy and the statistical rigour of flow cytometry in a single bench-top platform. According to QBI's Director of Flow Cytometry, Geoff Osborne, the Amnis ImageStream system provides a unique bridging technology between traditional flow cytometric techniques and imaging technologies. "This instrument is facilitating QBI's research efforts in understanding the fundamental characteristics of neural cells," Mr Osborne said. "The 'high content' nature of the data, which links morphological features to fluorescence profiles, is allowing new insights in these research areas."



▲ Data obtained using the unique bridging technology – new-generation flow cytometry. Glioblastoma cell lines are stained for GFAP (psuedo-coloured green) and DRAQ5 (psuedo-coloured pink), showing cells undergoing mitosis.

Photo: Chris Stacey, UQ

▲ Imaging specialist Damien Gardiner operating QBI's cell sorter.

HIGH-FIELD MAGNETIC RESONANCE IMAGING

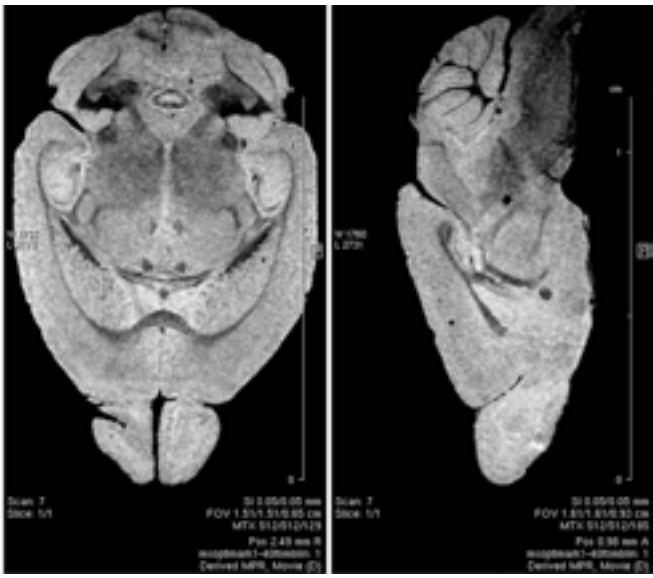
MRI is paramount to enhance the understanding of tissue structures, cellular metabolism and physiological response to disease and drug therapy.

Magnetic resonance imaging (MRI) is a non-invasive technique which is used to visualise and to study the structure and function of living organisms *in vivo*. In the field of biological and medical research, MRI is paramount to enhance the understanding of tissue structures, cellular metabolism and physiological responses to disease and drug therapy. It is used for research at multiple levels, from the cellular, to animal models through to medical diagnostic imaging of humans.

The recently commissioned 16.4T MRI spectrometer is the only one of its kind in the southern hemisphere. QBI researchers will use this scanner to study various neurological and developmental diseases in animal models for understanding pathophysiological changes at the microscopic level.

The Bruker Ultrashield Plus 700 WB Avance NMR spectrometer has a vertical open-bore diameter of 89 mm. After the positioning of gradient, shim and transmit/receiver coils, it provides a space of up to 34 mm diameter, which is optimal for mouse/small rat brain imaging.

The scanner is equipped with strong gradient inserts (up to 25mT/m/A), which enable atypical high-resolution imaging of brain structure in live animals (*in vivo*) at a sub-100 micron in-plane and in-depth ($<100\ \mu m)^3$ resolution. A higher (sub-30 $\mu m)^3$ resolution is typically attainable for *ex-vivo* samples.

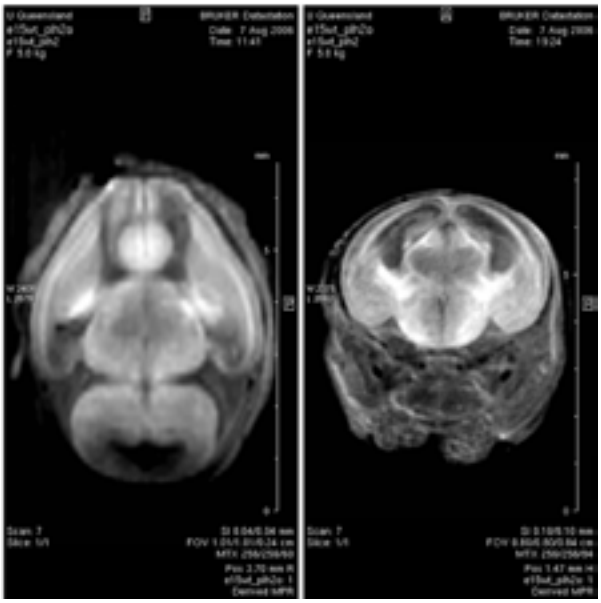


▲ 3D-spin echo of mouse brain. The acquisition parameters are TR/TE= 1500/13ms, 1 scan, acquisition time ~2.5h, at 117 x 140 x 280 μm^3 resolution using the 16.4T scanner.

To achieve highest sensitivity, the scanner will be equipped with new generation SAW/ quadrature micro-imaging coils (5, 10 and 20 mm diameters), suitable for imaging of excised brain, spinal cord and embryos. For live mouse imaging, the scanner is equipped with proton and dual frequency proton-fluorine transmit/receiver coils with a dedicated mouse bed/restraint apparatus. The dual proton-fluorine coil will permit the visualisation of ^{19}fluorine contrast agents, analogous to those commonly used in PET imaging.

The current 16.4T configuration is up to four times more sensitive than the 4.6T system, providing a faster scan time at a similar sub-100 micron resolution. This scanner will play an important role in a range of QBI research projects, e.g. detection of developmental brain abnormalities, structural and metabolic changes of mutant/transgenic mice, and the efficacy of treatments in spinal cord injury and stroke. It will also be used in the development of novel contrast agents and visualisation of gene activity by means of promoter-driven ferritin expression.

▲ QBI's Dr Nyoman Kurniawan, one of the many scientists who will use the 16.4T MRI system – a world-first configuration of state-of the-art imaging technology purchased with the assistance of Queensland Government Smart State Funding.



▲ High resolution image of excised head/brain of an E15 mouse embryo (40 x 40 x 120 μm^3). The image was acquired using a 3D-fast spin echo (TurboRARE) sequence (TR/TE= 3s/50ms, 6 scans, acquisition time ~20h) at 16.4T.

▲ *The new 16.4T MRI wide-bore spectrometer is one of only five such machines anywhere in the world.*

Photo: Chris Stacey, UQ

FUTURE DIRECTIONS

The Queensland Brain Institute looks to the future to build strategic relationships with knowledge partners, and to remain responsive to emerging scientific discoveries both in Australia and internationally.

As the neuroscience community's knowledge expands, related disciplines emerge as legitimate areas for fundamental research.

To maintain the Queensland Brain Institute's position as a centre of neuroscience excellence, the Institute plans to expand its focus to include several additional fields.

Recently, this expansion has included establishment of research laboratories in cognitive and behavioural neuroscience and vision.

PROFESSOR JASON MATTINGLEY BSc (Hons), MSc, PhD, MAPS

Neuroscientist and clinical neuropsychologist Professor Jason Mattingley joined QBI in late 2006. Professor Mattingley is recognised internationally for his research and extensive publication in cognitive neuroscience.

A central research theme for Professor Mattingley is his ongoing investigation into the mechanisms of selective attention, which are crucial to virtually all aspects of everyday behaviour and cognition.

His research aim is to address two broad questions concerning the nature of human selective attention. First, how does the brain filter sensory stimuli so that only behaviourally relevant inputs are selected for further processing? Second, what are the consequences of such selective processing for conscious perception and action?

At QBI, Professor Mattingley will address these questions from a number of perspectives, by studying individuals with acquired and developmental disorders of attention, such as spatial neglect and attention deficit hyperactivity disorder (ADHD), by using functional brain-imaging techniques such as fMRI, ERPs and near-infrared spectroscopy, to examine the neural correlates of attentional processes, and by applying transcranial magnetic stimulation (TMS) to focally stimulate regions of the brain thought to be involved in attentional control.

His research has important implications for real-world endeavours, including the diagnosis and treatment of individuals with attention deficits due to brain disease, and the design of more efficient systems for conveying information to human operators.

PROFESSOR MANDYAM SRINIVASAN FAA, FRS

INAUGURAL AUSTRALIAN FEDERATION FELLOW

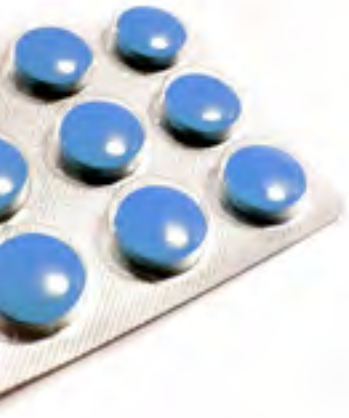
In early 2007, Professor Mandyam Srinivasan, recipient of the 2006 Australian Prime Minister's Prize for Science, joined QBI to expand his research into visual processing.

By studying the behaviour of small animals, such as insects, Professor Srinivasan has already demonstrated that many relatively simple nervous systems nevertheless display a rich behavioural repertoire. His research seeks to elucidate principles of flight control and navigation, and to explore the limits of the 'cognitive' capacities of small brains.

According to Professor Srinivasan, an understanding of visual processing in insects may provide simple, novel solutions to problems in machine vision and artificial intelligence.

Thus, another focus of his research is the design of biologically inspired algorithms for 'seeing' machines, and the development of autonomously navigating robots.

◀ As part of preparations to facilitate Professor Srinivasan's ongoing research into honeybee vision, a bee house has been constructed on the top floor of the Sir William MacGregor Building. The secure area has space for bee flight paths and hives.



INNOVATION AND COMMERCIAL OPPORTUNITIES

QBI has a responsibility to manage and protect any commercial application of the Institute's discoveries.

In many ways, the targeted and systematic approach QBI brings to the discovery process ensures commercial opportunities are never far behind our frontline research efforts.

QBI has engaged UniQuest to translate its neuroscience research into knowledge based, high-value commercial opportunities.

QBI researchers have identified key factors which have the potential to prevent loss of neurons or to replace lost neurons.

More than 100 million people suffer from some disorder of the brain or nervous system. Brain-related disorders account for the majority of the industrialised world's long-term care costs and, when combined with psychiatric disorders, account for more hospitalisation and prolonged care than almost all other diseases combined. Neurodegenerative diseases are expected to become the world's second leading cause of death by 2040, overtaking cancer.

Numerous neurological disorders such as Alzheimer's disease, Parkinson's disease, stroke, Huntington's disease and depression are associated with a reduction in the number of neurons. QBI researchers have identified key factors which have the potential to prevent loss of neurons or to replace lost neurons. Along the way, QBI has developed several new research tools to use in its quest to unravel the mysteries of the brain, some of which it has patented.

PREVENTING CELL DEATH

The p75 neurotrophin receptor has previously been implicated as a mediator of cell death in neurodegenerative conditions. QBI researchers have revealed that a region of the receptor, referred to as the 'Chopper domain', is critical for inducing cell death.

Researchers have also identified a cell membrane potassium channel which, when blocked, prevents p75 neurotrophin receptor-induced cell death.

An opportunity exists for investors to fund drug screening of these biological targets and therapeutic development.

NEURON REPLACEMENT

Building on the knowledge that the adult brain does contain stem cells and is capable of producing new neurons, QBI researchers have identified several factors involved in the proliferation, differentiation and migration of stem cells to sites in need of repair. QBI is working to apply these findings to the generation of new therapeutics for the treatment of conditions associated with neuron loss.

SPINAL CORD REPAIR

There are more than 300 new cases of spinal cord injury in Australia each year. QBI scientists, in collaboration with researchers from CSL Limited, the University of Melbourne and elsewhere in The University of Queensland are working together to develop a therapeutic to stimulate the repair of a newly damaged spinal cord.

MORE INFORMATION

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SECTION THREE

3

QBI EVENTS

The imaging centre's state-of the-art microscopes will be used for research that seeks to understand the fundamental mechanisms that regulate brain function.

▲ **(L– R)** Carl Zeiss Australasia Managing Director Tony Saliba, Professor Perry Bartlett, Professor David Siddle and Carl Zeiss MicroImaging executives, Dr Stefan Friedrichowski and Dr Solveig Hehl.

QUEENSLAND BRAIN INSTITUTE AND **ZEISS AUSTRALASIA** TO DEVELOP ADVANCED IMAGING TECHNOLOGY IN BRISBANE

The Queensland Brain Institute and international technology company Zeiss Australasia have agreed to develop high-end microscopy at The University of Queensland.

A Zeiss-equipped Advanced Imaging Centre – valued at more than $1.5 million – will be part of the new QBI neuroscience facilities which are due for completion by November 2007.

QBI Director, Professor Perry Bartlett said: "The new centre will enable QBI to become the focus for the development and application of new imaging technology within the Asia Pacific region, and will provide, together with the newly installed 16.4 Tesla MRI instrument, the resources for the next wave of discoveries in the neurosciences."

"It is also a pleasing recognition by a leading international scientific company of Australia's central role in the burgeoning scientific development in the Asia–Pacific region," Professor Bartlett said.

Zeiss Australasia Managing Director Tony Saliba said the new Advanced Imaging Centre was the first such arrangement in the Asia–Pacific region for his company.

"From our point of view, this is a long-term and strategic investment in partnership with a high-profile institute that we think will become the hub of neuroscience in the Asia–Pacific region", Mr Saliba said.

QBI's Professor Pankaj Sah said the imaging centre's state-of the-art microscopes would be used for research that seeks to understand the fundamental mechanisms that regulate brain function.

"It's anticipated that our increasingly detailed awareness of the cellular and molecular mechanisms underlying brain function will have a major impact on our understanding of more complex areas such as behaviour, cognition, ageing, neurological disease and mental illness," Professor Sah said.

LESS TRAVEL REQUIRED

"Until now, neuroscientists who wanted to develop research techniques at the highest levels of microscopy were obliged to travel to one or two centres in the United States or Europe."

"Instead of negotiating our technical requirements with sales representatives, we'll have a Zeiss specialist working with QBI neuroscientists, which means QBI gets the first 'hit' in terms of developing new technologies."

▲ QBI's Professor Pankaj Sah and Dr Zac Pujic with the Institute's latest Zeiss confocal microscope.

Under the agreement with Zeiss Australasia, the imaging centre will be staffed by a Zeiss-trained product specialist to work with scientists in the development and application of advanced imaging technologies.

In addition, Zeiss Australasia and QBI are developing travelling fellowships to encourage collaboration with early- to mid-career scientists, particularly from China.

QBI **NEUROSCIENCE EVENTS**

Our understanding of the mechanisms regulating brain function has undergone a revolutionary change in recent years ...

▲ Speakers at QBI's inaugural Brain Plasticity Symposium: **(front row L–R)** Jack Kessler, Pankaj Sah, Susumu Tonegawa, Perry Bartlett, **(back row L-R)** Helen Cooper, Seong-Seng Tan, Bai Lu, Tony Hannan, Macdonald Christie, Roger Nicoll, Elizabeth Coulson, Mandyam Srinivasan, Brent Reynolds, Linda Richards, Rod Rietze, Peter Mombaerts

INAUGURAL **QBI BRAIN PLASTICITY** SYMPOSIUM

QBI's inaugural Brain Plasticity Symposium in September 2005 attracted 25 of the world's leading neuroscientists, including Nobel Laureate Professor Susumu Tonegawa from the Massachusetts Institute of Technology.

QBI Director Professor Perry Bartlett said it was an indication of QBI's international standing that it was able to attract so many top researchers to speak at the symposium.

"We hope to establish this as the premier meeting in the area of brain plasticity, with the next symposium scheduled for 2008," Professor Bartlett said.

SECOND **PACIFIC RIM BRAIN CONFERENCE**

Aimed at promoting links between members of the Pacific Rim research community, the biennial Pacific Rim Brain Conference in 2006 highlighted current advances in neuroscience.

The meeting opened with the latest developments in imaging and computational neuroscience, followed by presentations from leaders in the fields of epilepsy, cognitive neuroscience and animal models of brain injury and disease.

Guest speakers included leading scientists from the RIKEN Brain Science Institute (Shun-ichi Amari and Kazuhiro Yamakawa), neurologists in the fields of cognition (Jason Mattingley) and epilepsy (David Reutens), and world leaders in the development of imaging techniques (Zang-Hee Cho) and computational neuroscience (Peter Dayan).

The mix of scientists and small size of the conference promoted vibrant discussions throughout the meeting and has lead to new collaborations between UQ and the RIKEN Brain Science Institute.

AUSTRALIA'S FIRST WORKSHOP IN **MATHEMATICAL** AND **COMPUTATIONAL NEUROSCIENCE**

Mathematical and Computational Neuroscience aims to understand how biological nervous systems process information by modelling them at scales including the biophysical, circuit and systems level.

QBI's inaugural workshop in mathematical and computational neuroscience in August 2006 provided, for the first time in Australia, an opportunity for scientists to survey the current state of this rapidly expanding area of neuroscience.

Coordinated by QBI's Associate Professor Geoffrey Goodhill, the one-day workshop attracted researchers from Japan, USA, UK and Australia, and featured a line-up of eminent researchers in mathematical and computational neuroscience.

▲ Eminent researchers from Japan, USA and Australia attended QBI's inaugural workshop in mathematics and computational neuroscience in August 2006: **(L–R)** Shun-ichi Amari, Geoff Goodhill, Peter Dayan, Peter Robinson, Tony Burkitt, Li Zhaoping, Kevin Burrage, Mandyam Srinivasan

AUSTRALIAN COURSE IN **ADVANCED NEUROSCIENCE**

Since 2005, QBI's Professor Pankaj Sah has helped to coordinate the Australian Course in Advanced Neuroscience (ACAN) at The University of Queensland's Moreton Bay Research Station on Stradbroke Island, off the coast of Brisbane.

The program is Australia's answer to the legendary neuroscience training programs held at Woods Hole and Cold Spring Harbor in the USA. ACAN follows a similar format to these advanced neuroscience education programs.

During the three-week course, participants have an opportunity to learn and work in small groups with leading Australian and overseas scientists. For many early career neuroscientists, the program is a useful way to master new disciplines and experimental techniques.

As well as attending lectures about the fundamentals of cellular neuroscience, participants receive extensive hands-on laboratory training with the latest equipment and conduct a research project of their own choosing.

(back row L–R): Jeff Maclean, David Merson, Bob Atkinson, John Lyons, John Hay, Perry Bartlett, Leigh Matthews, John Kelly, **(centre)** Sallyanne Atkinson

COMMUNITY LEADERS BEHIND NEUROSCIENCE RESEARCH

Eight of Queensland's most talented and experienced business and community leaders have come together to map out a strategy that is destined to set the agenda for neuroscience research funding in the state.

Former Brisbane Lord Mayor Sallyanne Atkinson and the Queensland Police Commissioner Bob Atkinson joined business identities John Lyons, Jeff Maclean, Leigh Matthews and David Merson in a round-table session aimed at securing ongoing funding for neuroscience excellence at the Queensland Brain Institute.

QBI Director Professor Perry Bartlett said the collective professionalism and experience of the board members would be invaluable in setting the strategic external fundraising direction of the Institute.

"The University of Queensland and QBI have established the board to assist the strategic planning and development of the Institute," Professor Bartlett said.

"We expect the QBI Development Board to take a leadership role in any major fundraising campaign undertaken by QBI.

"It's anticipated that the board – with each member serving in an honorary capacity – will convene at least four times a year, assisting QBI in creating appropriate linkages to government, business and the wider community."

To date, establishment of QBI has been funded by charitable donations, government infrastructure grants and operational funds from The University of Queensland.

To maintain and expand its operation QBI will need to obtain continuing funding from UQ, as well as government research grants and other external sources.

UQ's Senior Deputy Vice-Chancellor Professor Paul Greenfield AO and Professor Bartlett are also members of the board, which met for the first time in September 2006.

Unusually dry conditions in Brisbane meant construction of QBI's new building continued almost uninterrupted since earthworks began in late 2005. With an official opening scheduled for November 2007, the seven-storey complex will bring QBI's laboratories together under one roof for the first time.

Dec 2005

April 2006

May 2006

June 2006

July 2006

Dec 2006

"We now know the brain is a highly plastic organ capable of making new connections and new nerve cells, even in the brain of an older person."
– Professor Bartlett

BRAIN BEE CHALLENGE – A FIRST FOR NEUROSCIENCE EDUCATION IN AUSTRALIA

With all the drama of a TV game show, the inaugural Australian Brain Bee Challenge began on Tuesday, 14 March 2006 with a rowdy cheer from some of the smartest teenagers in south-east Queensland and northern New South Wales.

More than 200 high school students from 30 schools participated, in teams and as individuals, while many more came along to support their science students in action.

'Pumped up' on neuroscience – and legions of their cheering school mates – the contestants battled in an impressive test of neuroscience knowledge.

But this was no frivolous talent show; the crowd, the emotions and the competition had all the ingredients of a gladiatorial stoush to the end.

Organised by the Queensland Brain Institute and the Faculty of Biological and Chemical Sciences, the Brain

IMPROVING PUBLIC AWARENESS OF MOTOR NEURON DISEASE

As part of Motor Neuron Disease awareness week, the Queensland Brain Institute (QBI) and the Motor Neuron Disease Association of Queensland (MNDAQ) coordinated a public information seminar in April 2006.

Motor neuron disease is the name given to a group of diseases in which the nerve cells that control the muscles degenerate and die.

▼ QBI scientists take part in an MND Awareness Week public seminar at UQ's Customs House.

QBI Director Professor Perry Bartlett delivered a public lecture on MND at UQ's Customs House.

Professor Bartlett said the past decade of neuroscience research had led to a radical change in the science community's understanding of how the brain functions.

"We now know the brain is a highly plastic organ capable of making new connections and new nerve cells, even in the brain of an older person, in response to a variety of stimuli," Professor Bartlett said.

"We now believe that it is this plasticity which underpins higher brain functions such as memory and learning."

QBI scientists have recently made significant advances in understanding how to promote new nerve cell production, prevent nerve cell death, and promote nerve cell re-connection, which may have significant impact on future therapies for diseases such as MND.

Professor Bartlett highlighted these new findings and how they may be applied to treating MND.

In 2005, QBI scientist Dr Robyn Wallace was awarded the Ross Maclean Fellowship for further study into MND.

▲ Professor Mick McManus (left) and Professor Perry Bartlett congratulate Tim Mew, the 2006 Australian Brain Bee Challenge individual competition winner.

▲ ABBC Individual Competition runner-up, Katelin Haynes (West Moreton Anglican College).

Bee Challenge was the first major neuroscience competition for high school students staged in Australia.

To the amazement of the judges and audience members alike, the students appeared to grow taller and wiser with every question.

Event coordinator and Queensland Brain Institute Associate Professor Linda Richards said she was awestruck at the depth and complexity of neuroscience knowledge many of the students had demonstrated.

"Such enthusiasm is a great credit to science teachers and an indication of the growing importance and relevance of neuroscience to the whole community," Dr Richards said.

"The Brain Bee Challenge is more than a competition to see who knows the most about the brain. For many students it was also their first opportunity to see research laboratories first-hand and to talk to scientists about their work."

"The Queensland Brain Institute believes it should be proactive in encouraging the best and brightest students to consider a career in neuroscience," Dr Richards said.

2006 AUSTRALIAN BRAIN BEE INDIVIDUAL WINNERS

1 **Timothy Mew** (St Paul's School, Brisbane)

2 **Katelin Haynes** (West Moreton Anglican College, Ipswich)

3 **Kathryn Noakes** (St Paul's School, Brisbane)

4 **James Bennett** (St Paul's School, Brisbane)

5 **Sohum Banerjea** (Merimac State High School, Mermaid Waters)

2006 AUSTRALIAN BRAIN BEE TEAM WINNERS

1 **Somerset College** (Mudgeeraba)

2 **Trinity College** (Lismore)

3 **Redlands College** (Wellington Point)

4 **St Paul's School** (Bald Hills)

Professor Takeichi studies the mechanisms by which animal cells recognise one another and form selective bonds with appropriate cells.

TOSHIYA YAMADA MEMORIAL LECTURE

▲ Presenter of the 2006 Toshiya Yamada Memorial Lecture, Professor Masatoshi Takeichi, who is Director of the Centre for Developmental Biology at the RIKEN Institute in Kobe, Japan.

About 150 scientists, interested members of the public and supporters attended the 2006 Toshiya Yamada Memorial Lecture presented by distinguished Japanese scientist, Professor Masatoshi Takeichi.

The memorial lecture – which has become a regular part of Brain Awareness Week – was coordinated by the Institute for Molecular Bioscience (IMB) and QBI.

Professor Takeichi is Director of the Centre for Developmental Biology at the RIKEN Institute in Kobe, Japan. His lecture, entitled 'Cells into organs: how multicellular systems form', examined how cancer spreads through the body and how cells organise themselves into complex tissues.

Professor Takeichi studies the mechanisms by which animal cells recognise one another and form selective bonds with appropriate cells. He has had a long and distinguished career, including being awarded one of only three 2005 Japan Prizes, often called Japan's Nobels. The lecture was named in memory of the late Dr Toshiya Yamada, who passed away in 2001. Dr Yamada was an IMB researcher whose discoveries formed much of the basis of modern neurobiology. Dr Yamada discovered the molecules that are essential for regulating the correct wiring of the spinal cord and parts of the brain, and was instrumental in the resurgence of Australia as a leader in the field of developmental neurobiology.

QBI's Associate Professor Dr Linda Richards presented the inaugural Toshiya Yamada Memorial lecture in March 2005.

SECTION FOUR

4

PEOPLE AND PUBLICATIONS

QBI PUBLICATIONS

Andrews W, Liapi A, Plachez C, Camurri L, Zhang J, Mori S, Murakami F, Parnavelas JG, Sundaresan V, Richards LJ (2006) Robo1 regulates the development of major axon tracts and interneuron migration in the forebrain. *Development* 133: 2243–2252.

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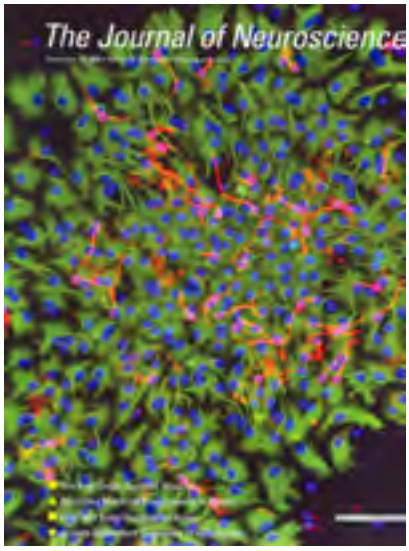

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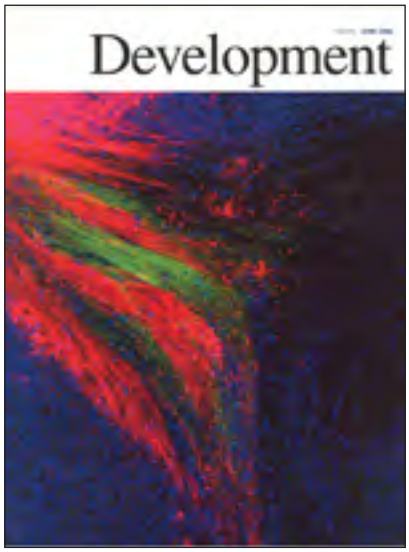

▲ **Andrews W, Liapi A, Plachez C, Camurri L, Zhang J, Mori S, Murakami F, Parnavelas JG, Sundaresan V, Richards LJ** (2006) Robo1 regulates the development of major axon tracts and interneuron migration in the forebrain. *Development* 133: 2243–2252

▲ **Vescovi AL, Galli R, Reynolds BA** (2006) Brain tumour stem cells. *Nature Reviews Cancer* 6: 425–436

Cover: Claudia Bentley, Nature Reviews Cancer, Macmillan Magazines Ltd.

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QBI NEUROSCIENCE **SEMINAR SERIES**

Since its foundation, the Queensland Brain Institute has played a leadership role in coordinating neuroscience seminars, designed to promote excellence through the exchange of ideas, establishing new collaborations and augmenting existing partnerships.

During the past four years, this program has been instrumental in attracting more than 100 high-profile scientists to Brisbane to share their neuroscience knowledge and experience with the wider UQ community.

The program also provides a unique opportunity for QBI scientists (and other members of the UQ community) to showcase their ideas to their international peers.

◀ *QBI Research Fellow Dr John Power delivering one of the more than 130 neuroscience seminars provided by the Institute during the past four years.*

2006 – QBI NEUROSCIENCE SEMINARS
(IN ORDER OF APPEARANCE)

Dr Patricia Yam (Stanford University), *Actin-myosin network reorganization in symmetry-breaking and spontaneous cell motility initiation.*

Assistant Professor Frederic Charron (Department of Medicine, Université de Montréal), *Morphogens as brain wiring molecules: identifying the molecular mechanism underlying Sonic hedgehog-mediated axon guidance.*

Dr Michael Piper (Queensland Brain Institute), *Regulation of retinal axon guidance in Xenopus.*

Dr Zac Pujic (Queensland Brain Institute), *Analysing the response of axons to molecular gradients.*

Professor Paul Martin (National Vision Research Institute of Australia, The University of Melbourne), *Subcortical channels for colour vision in primates.*

Dr Peter Papathanasiou (Department of Pathology, Stanford University), *Stem cells, mutants and epigenetics.*

Dr Robert Henderson (Royal Brisbane and Women's Hospital), *Markers of disease progression in MND.*

Assistant Professor Grant Mastick (Department of Biology, The University of Nevada), *Growing long and straight: mechanisms of longitudinal axon guidance.*

Dr Klaus Stiefel (Computational Neurobiology Laboratory, The Salk Institute), *Nonlinear dynamics in neural function.*

Associate Professor Graham Barrett (The University of Melbourne), *p75 – the anti-neurotrophic receptor.*

Associate Professor Marcello Rosa (Centre for Brain and Behaviour, Monash University), *What, if anything, is a cortical area? Lessons from comparative and developmental studies.*

Dr Dhanisha Jhaveri (Queensland Brain Institute), *To divide or survive: BDNF plays a role.*

Dr Nyoman Kurniawan (Queensland Brain Institute and Centre for Magnetic Resonance), *Biomarker development for magnetic resonance imaging.*

Professor Robert Rush (Department of Human Physiology, Flinders Medical Centre), *Targeted gene delivery into neurons.*

Professor Trichur Vidyasagar (Department of Optometry & Vision Sciences, The University of Melbourne), *Neural interactions in the primate cortex underpinning focal spatial attention.*

Professor Sharad Kumar (Hanson Institute and Institute of Medical and Veterinary Science), *Execution of apoptosis: lessons from flies and mammals.*

Dr Li Li (Queensland Brain Institute), *IFNgamma: a regulator of neural precursor activity.*

Associate Professor Helen Cooper (Queensland Brain Institute), *Neogenin regulates early vertebrate CNS development.*

Professor Bruce Crosson (University of Florida and The McKnight Brain Institute), *Differential neural substrates and treatment response in aphasia.*

Professor Justin Marshall (School of Biomedical Sciences, The University of Queensland), *Recent advances in seeing sexy partners.*

Dr Jennifer Rodger (University of Western Australia), *Topographic maps in the brain: how and why?*

Professor Glenda Halliday (Prince of Wales Medical Research Institute), *New ideas on the pathogenesis of Parkinson's disease.*

Dr Sally Firth (School of Pharmacy, The University of Queensland), *Interneurons isolated from the developing retina display spontaneous increases in intracellular calcium concentration.*

Professor Stephen Wood (Child Health Research Institute), *The neurobiology of USP9X – a 'stemness' gene.*

Dr Christopher Reid (Howard Florey Institute), *Cellular mechanisms involved in epilepsy.*

Professor William Ross (New York Medical College), *Calcium waves in pyramidal neurons.*

Professor Shaun Collin (School of Biomedical Sciences, The University of Queensland), *Insights into primitive behaviour: photoreception in lampreys and lungfishes.*

Professor Elspeth Maclachlan (Spinal Injuries Research Centre), *Inflammation after nerve injury – what kind of immune response?*

Dr Tara Walker (Queensland Brain Institute), *A transgenic approach to dissecting neurogenesis.*

Dr Vu Dang (Pain Management Research Institute), *Mu opioid receptor regulation and morphine tolerance.*

Dr John Power (Queensland Brain Institute), *Compartmentalisation of calcium responses in basolateral amygdala neurons.*

Professor Bronwen Connor (University of Auckland), *Adult neural progenitor cells and cell replacement therapy for neurological disease.*

Professor Leslie Rogers (University of New England), *From brain to behaviour: development and evolution of the lateralised brain.*

Dr Ross Cunnington (Howard Florey Institute), *The supplementary motor area and the readiness for action: studies of event-related functional MRI.*

Dr Tom Gonda (Centre for Immunology and Cancer Research, The University of Queensland), *Retroviral expression cloning and more: an overview of research in the Molecular Oncogenesis Group CICR.*

4 NEUROSCIENCE SEMINARS

Dr Rod Rietze (Queensland Brain Institute), *Regulation of neural stem cell activity by growth hormone receptor.*

Dr Sofia Frangou (Institute of Psychiatry, London), *Fitting bipolar disorder and schizophrenia in the psychosis puzzle.*

Dr Judith Reinhard and **Dr Charles Claudianos** (Australian National University), *Vision, olfaction and memory: lessons from the honeybee, and building a brain synapse: from enzyme to receptor.*

Dr Kirsty Spalding (Karolinska Institute, Stockholm), *Analysis of neuronal turnover in the adult human brain.*

Professor John Parnavelas (University College, London), *Mechanisms involved in the migration of cortical interneurons focusing on the role(s) of Slit/Robo interactions.*

Professor Mriganka Sur (Massachusetts Institute of Technology), *The rules of cortical plasticity.*

2005 – QBI NEUROSCIENCE SEMINARS

Professor Mandyam Srinivasan (Centre for Visual Sciences, The Australian National University), *Picking a bee's brain: insights into vision, navigation, 'cognition' and robotics.*

Dr Philip Poronnik (School of Biomedical Sciences, The University of Queensland), *Nedd4 and NHERF: intracellular regulators of epithelial transport and beyond.*

Professor Mick Brammer (King's College London), *Functional magnetic resonance imaging in psychiatry.*

Dr Andrew Lawrence (Howard Florey Institute), *Therapeutics for alcoholism: what's the future?*

Dr Andrew Delaney (Queensland Brain Institute), *Kainate receptors modulate release at two parallel fibre synapses in cerebellum.*

Dr Roberto Cappai (University of Melbourne), *Alzheimer's disease: the role of the amyloid precursor protein and amyloid beta peptide in disease and health.*

Dr Christine Neyt (Queensland Brain Institute), *Expression of the neurotrophin receptor p75 in the subventricular zone (SVZ) and rostral migratory stream (RMS).*

Professor Bob Foehring (University of Tennessee), *Diversity and function of Kv1 channels in pyramidal neurons.*

Dr Jacqueline Matthews (University of Sydney), *Assembly of LIM-containing regulatory protein complexes.*

Dr Simon Murray (University of Melbourne), *The 'Chopper' domain regulates NGF binding and signalling.*

Dr Greg Stuart (John Curtin School of Medical Research, Australian National University), *Properties and function of HCN channels in physiology and pathology of CNS.*

Professor Chris Goodnow (Australian Phenomics Facility), *Translating the genome into the phenome.*

Professor Peter Dunkley (University of Newcastle), *Novel mechanisms for receptor-mediated control of catecholamine synthesis.*

Professor Jason Mattingley (Department of Psychology, University of Melbourne), *Attentional modulation of visual perception.*

Dr Clarke Raymond (John Curtin School of Medical Research, Australian National University), *Location, location: spatial segregation of neuronal calcium.*

Professor Wayne Hall (Institute for Molecular Bioscience, The University of Queensland), *Genetic and neuroscience perspectives on addiction: ethical and policy implications.*

◀ (R-L) Visiting lecturer Dr Ross Cunnington (Howard Florey Institute) with QBI Director Professor Perry Bartlett.

Dr John Bekkers (John Curtin School of Medical Research, Australian National University), *Neural processing in the primary olfactory cortex.*

Dr Robert Callister (University of Newcastle), *Sensory processing in spinal cord pain circuits* in vivo.

Dr Mark Bellingham (School of Biomedical Sciences, The University of Queensland), *The final common pathway.*

Dr Elizabeth Coulson (Queensland Brain Institute), *Signalling neuronal death through the neurotrophin receptor.*

Dr Robyn Wallace (Queensland Brain Institute), *Molecular genetics of epilepsy.*

Dr Richard Masland (Harvard University), *Multiple parallel outputs from retina to brain.*

Dr Richard Banati (University of Sydney), *Neuron-glia interaction in brain disease: neuroimaging results on microglial activation.*

Professor Hugh Wilson (York University, Canada), *Perceptual oscillations and waves in vision.*

Mr Tom Keeble (Queensland Brain Institute), *Characterisation of the role Ryk in the mammalian brain.*

Professor Alan Harvey (University of Western Australia), *The combined use of transplantation and gene therapy in visual system repair.*

Dr Marc Hauser (Harvard University), *The auditory world of primates*: *from behaviour to brain and back again.*

Dr Sam Morley (Queensland Brain Institute), *Neurotrophin regulation of zinc toxicity.*

Professor Clive Harper (University of Sydney), *The neurotoxicology of alcohol.*

Dr Gary Egan (Howard Florey Institute), *High resolution structural and functional MR maps of the human sensorimotor system.*

Associate Professor Linda Richards (Toshiya Yamada Memorial Lecture – Queensland Brain Institute and School of Biomedical Sciences, The University of Queensland), *Wiring the brain: how connections form during development.*

Dr Phil Crozier (University of Auckland), *Uncovering Runx gene function using zebrafish genetics.*

4 NEUROSCIENCE SEMINARS

Dr Paul Beatus (Queensland Brain Institute), *Oncastatin M, the forgotten cytokine: the effects of oncostatin M on adult neural progenitors.*

Dr Allan Gulledge (Australian National University), *Cholinergic inhibition of neo.*

Professor Nadia Rosenthal (Head of European Molecular Laboratory – Monterotondo Outstation and Co-ordinator Mouse Biology Unit EMBL, Italy), *Growth factor enhancement of mammalian regeneration.*

Dr Peter Bailey (Karolinska Institute, Sweden), *A global genomic code for gene expression within the vertebrate CNS.*

Associate Professor Joe Lynch (School of Biomedical Sciences, The University of Queensland), *Molecular mechanisms of picrotoxin action at the glycine receptor.*

2004 – QBI NEUROSCIENCE SEMINARS

Dr Brent Reynolds (Queensland Brain Institute), *Neural stem cells and the neurosphere assay: a decade of erroneous results?*

Dr Richard Carson (School of Human Movement Studies, The University of Queensland), *Neural pathways mediating interlimb coordination.*

Dr Sam Morley (Queensland Brain Institute), *Neurotrophin and cytokine and regulation of zinc neurotoxicity.*

Professor David Burr (Instituto di Neuroscienze del CNR, Italy), *Saccades cause relativistic compression of time as well as space.*

Dr Louise Faber (Queensland Brain Institute) *Cells and circuitry in the lateral amygdala: the cellular basis of emotional processing.*

Professor Lyn Beazley (University of Western Australia), *Molecular and behavioural prerequisites for central nerve regeneration.*

Professor Kirk Jensen (University of Adelaide), *Targeting the processes – Identifying RNA-Protein interactions important for neuronal function.*

Associate Professor Lea Williams (Brain Dynamics Centre, Westmead Hospital), *'Affective' neuroscience and neuroimaging: a focus on PTSD.*

Mr Toby Merson (Walter and Eliza Hall Institute), *The histone acetyltransferase querkopf controls adult neurogenesis by regulating neural stem cells.*

Professor George Paxinos (Prince of Wales Medical Research Institute), *Brain, behaviour and evolution.*

Professor Robert Saint (Australian National University), *Pebble thrown into GTPase pond makes waves*.

Dr James St John (School of Biomedical Sciences, The University of Queensland), *Is axon targeting in the olfactory system system more complex than we thought?*

Dr John Drago (Howard Florey Institute and Consultant Neurologist, St Vincent's Hospital), *Sprouting in doaminergic neurons: interactions between dopamine receptors, dopamine transporters and nicotinic receptors.*

Dr Rod Murphey (Biology Department, University of Massachusetts), *Synapse formation and degradation in the Drosophila system.*

Professor Chen Chen (Prince Henry's Institute of Medical Research), *Receptor, ion channel, and signalling in pituitary somatotropes.*

Dr Filip Lim (Department of Molecular Biology Universidad Autonoma de Madrid, Spain), *Reverse genetics in the development of nervous system therapies.*

Professor Martin Lavin (Queensland Institute of Medical Research & Central Clinical Division, School of Health Sciences, The University of Queensland), *Importance of DNA damage response in neurodegenerative disorders.*

Professor Fred Westbrook (School of Psychology, University of New South Wales), *Attentional learning in Pavlovian fear conditioning: the possible role of dopamine in the accumbens nucleus.*

Professor Graeme Jackson (Brain Research Institute, Austin Health), *Physiology & MR.*

Professor John Saunders (Alcohol and Drug Studies, The University of Queensland & Alcohol and Drug Service), *The nature, causes and consequences of addiction.*

Associate Professor Peter Kaye (School of Biomedical Sciences, The University of Queensland), *Cytokines and the beginnings of development and differentiation in mammals.*

Professor Stuart Crozier (School of Information Technology & Electrical Engineering, The University of Queensland), *Is MRI of the human brain possible at 11T?*

Professor Peter Koopman (Institute for Molecular Bioscience, The University of Queensland), *Sox genes: Key regulators of cell phenotype.*

Dr Peter Noakes (School of Biomedical Sciences, The University of Queensland), *The cell and molecular mechanisms underlying motor neuron survival during development.*

Professor Andrew Boyd (Leukaemia Foundation Laboratory, Queensland Institute of Medical Research), *The nature and consequences of Eph-ephrin interactions.*

Dr Warren Alexander (Walter and Eliza Hall Institute), *SOCS proteins.*

Mr Geoff Osborne (John Curtin School of Medical Research, The Australian National University), *Flow cytometric applications and future directions.*

Dr Gavan McNally (University of New South Wales), *The regulation of Pavlovian association formation.*

Dr David Walker (Department of Neurosurgery, Royal Brisbane Hospital), *Malignant brain tumours – current and future therapies.*

Dr Theo Mantamadiotis (Peter MacCallum Cancer Centre), *Dissecting transcriptional networks regulating neurogenesis in the adult brain.*

Professor Felix Viana (Instituto de Neurosciencias, Universidad Miguel Hernandez/CSIC, Spain), *Feeling cool: cellular mechanisms of cold temperature transduction in mammalian sensory neurons.*

Professor Anthony-Samuel La Mantia (University of North Carolina), *Induction and the specification of cell classes in the mammalian olfactory pathway.*

2003 – QBI NEUROSCIENCE SEMINARS

Dr John Power (Queensland Brain Institute), *Subliminal calcium signalling.*

Associate Professor Ottmar Lipp (School of Psychology, The University of Queensland), *Blink reflexes as probes for emotion and attention.*

Professor Mandyam Srinivasan (Centre for Visual Sciences, Research School of Biological Sciences, Australian National University), *Small brains, smart minds: honeybee vision, navigation and 'cognition'.*

4 NEUROSCIENCE SEMINARS

Professor Alun Davies (Department of Preclinical Veterinary Studies, Royal School of Veterinary Studies, Edinburgh), *Growth factors and growth factor signalling in sympathetic neuron development.*

Dr Daniel Peet (School of Molecular & Biomedical Science, *The University of Adelaide), Hypoxia, HIFs and hydroxylases: making sense of oxygen sensing.*

Professor Max Coltheart (Macquarie Centre for Cognitive Science, Macquarie University), *The cognitive neuropsychology of delusional belief.*

Professor John Bixby (Neuroscience Centre, The Miami Project to Cure Paralysis, University of Miami), *Receptor tyrosine phosphatases in vertebrate axon growth.*

Dr Stephen Rose and **Dr Simon Finnigan** (Centre for Magnetic Resonance, The University of Queensland), *MRI and EEG in stroke.*

Professor Michael Humphreys FAASA (Centre for Human Factors and Applied Cognitive Psychology, The University of Queensland), *Is the source of noise in recognition the same as it is in recall?*

Dr Guy Wallis (School of Human Movement Studies, The University of Queensland), *Learning to recognise objects.*

Associate Professor Bryan Mowry (Queensland Centre for Schizophrenia Research, The Park Centre for Mental Health), *Latest findings in the hunt for schizophrenia genes*.

Ms Sonya Kleinlogel (Vision, Touch and Hearing Research Centre, School of Biomedical Sciences, The University of Queensland), *The astonishing colour and polarisation vision system of the mantis shrimp.*

Professor Max Bennett (Neurobiology Laboratory, Department of Physiology, The University of Sydney), *On the plasticity of single synapses.*

Dr Ryszard Maleszka (Research School of Biological Sciences, The Australian National University), *The honeybee neurogenomics: From molecules to behaviour.*

Professor John McGrath (Queensland Centre for Schizophrenia Research, The Park Centre for Mental Health, Queensland), *The causes of schizophrenia: some recent results and some speculation.*

Professor Pankaj Sah (Queensland Brain Institute), *Synaptic transmission in the basolateral amygdala.*

Dr Kathryn Buller (School of Biomedical Sciences, The University of Queensland), *Conversations between the brain and the immune system.*

Dr Margie Wright (Queensland Institute of Medical Research), *Tying variation in our genes to brain processes: the Brisbane twin cognition study.*

Dr Monica Hurdal (Department of Mathematics, Florida State University), *Angle-preserving (conformal) flat maps of the human brain.*

Dr James Tresilian (School of Human Movement Studies, The University of Queensland), *Eye-hand coordination in space-time.*

Professor Peter Mombaerts (Laboratory of Developmental Biology & Neurogenetics, The Rockefeller University), *Olfaction targeted!*

Dr Peter Dodd (Biochemistry Department, The University of Queensland), *Massive attacks: microarrays, proteomics, tissue arrays and the human alcoholic brain.*

Dr Helmut Butzkueven (The Walter and Eliza Hall Institute), *Oligodendrocyte-specific therapy for multiple sclerosis?*

Associate Professor Shaun Collin (School of Biomedical Sciences, The University of Queensland), *Environmental and evolutionary clues to the prehistoric origins of colour vision*.

Ms Kaylene Young (Queensland Brain Institute), *Another function for the p75 neurotrophin receptor: its influence on stem cell activity and differentiation.*

Dr Helen Cooper (Queensland Brain Institute), *Diverse roles of netrin receptors in central nervous system development.*

Professor Richard Ivry (Institute of Cognitive and Brain Sciences, University of California, Berkeley), *Timing, temporal coupling and the selection of action.*

Dr Rodney Rietze (Queensland Brain Institute), *Adult neural stem cells: purification, potential and pitfalls.*

Associate Professor Justin Marshall (Vision, Touch and Hearing Research Centre, The University of Queensland), *From photoreceptor to satellite: an over-holistic approach to vision.*

Professor Jack Pettigrew (Vision, Touch and Hearing Research Centre, The University of Queensland), *Perceptual oscillation and psychosis.*

Professor David Hume (Institute for Molecular Bioscience, The University of Queensland), *The mononuclear phagocyte system and the brain.*

Dr Ann Turnley (Centre for Neuroscience, University of Melbourne), *SOCS-2 is a potent regulator of neuronal differentiation and neurite outgrowth.*

Professor Colin Masters (University of Melbourne), *Testing the A-beta amyloid theory of Alzheimer's disease.*

Professor David Hunt (Institute of Ophthalmology, University College of London) *Inherited retinal disease: functional analysis of disease proteins.*

Associate Professor Tony Hannan (Howard Florey Institute), *Gene-environment interactions mediating cortical plasticity in Huntington's disease transgenic mice.*

Professor Alan Mackay-Sim (Centre for Molecular Neurobiology, Griffith University), *Adventures up the nose: from the lab to the clinic.*

Dr Anne Lingford Hughes (Division of Psychiatry, University of Bristol), *Using neuroimaging to unravel the neurobiology of addiction.*

Dr Elizabeth Coulson (Queensland Brain Institute), *p75NTR-mediated neuronal death is regulated by synaptic activity modulating GIRK channels.*

Professor Jonathan Raper (Department of Neuroscience, School of Medicine, University of Pennsylvania), *Roles of Semaphorins and their receptors during development.*

Dr Peter Crack (Centre for Functional Genomics and Human Disease, Monash University), *The use of functional genomics in the understanding of stroke.*

Dr Paul Beatus (Queensland Brain Institute), *Notch in development and disease: a molecular dissection.*

QUEENSLAND BRAIN INSTITUTE
RESEARCH STAFF 2006

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Dr Geoffery Ericksson

Dr Louise Faber

Associate Professor Geoffrey Goodhill

Professor John McGrath

Mr Geoff Osborne

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Tim Butler, *BSc (Hons)*

4 QBI OPERATIONAL STAFF

▲ Deputy Director (Operations) John Kelly

The building, scheduled for completion in August 2007, will enable the Institute to become one of the finest neuroscience facilities in the world.

QBI **OPERATIONS** AND **SUPPORT**

In November 2003, the Queensland Brain Institute (QBI) was established by The University of Queensland Senate as a research institute, reporting directly to the Senior Deputy Vice-Chancellor, Professor Paul Greenfield. The establishment of QBI arose from a vision to create an environment of world-leading neuroscientists that worked on a common theme of "Understanding how the brain works". The University appointed Professor Perry Bartlett FAA as the inaugural Director of QBI and Mr John Kelly as Deputy Director (Operations).

As QBI developed its research base, the University provided recently refurbished space in the Ritchie building to accommodate the expanding number of scientists. This space provided facilities to support an array of research functions and core technologies such as flow cytometry and imaging. The current staff complement operating out of the Ritchie research facility is about 80 (scientists and operational staff). To support the concept of building research capacity in Queensland and at the University, 73 of the QBI staff are new to Queensland; indeed, 50 per cent of these were recruited internationally.

OPERATIONS

While building its capacity, QBI has worked operationally alongside established organisational units, namely the School of Biomedical Sciences and the Faculty of Biological and Chemical Sciences. Their commitment and invaluable support in establishing the Institute is gratefully acknowledged. This strategy allowed QBI to operate as an institute while developing critical mass in both the scientific and operational areas. To date, QBI has established the following operational units:

- **Research Management** (Rowan Tweedale) coordinates research grant applications, reviews grants and manuscripts and provides advice for funding schemes and research opportunities.
- **Projects and Development** (Alison van Niekerk) coordinates development through specific projects, including government and international relations, and manages the activities of the Communication, Development and Events sections.
- **Finance Section (Katherine Parsonage)** manages the Institute's financial services, including goods-received and (from 2007) the consumables store.

▼ **Operations staff: (L–R)** Ron Hohenhaus, Annita Nugent, Rowan Tweedale, Helen Staunton, Shani Doig, Charmaine Paiva, Veronica Baldry, John Kelly.

* Absent: Alison van Niekerk

▼ **Information Technology**: **(L–R)** Ian Duncan and Jake Carroll.

- **Human Resources** (Helen Staunton) administers the QBI human resources, including Research Higher Degree and postdoctoral support services.
- **Administration Support Services** (Veronica Baldry and Charmaine Paiva) provide the necessary administrative support for the operations of QBI and the Executive.
- **Information Technology** (Ian Duncan) manages the information technology unit in QBI. This is a joint position with the Australian Institute of Bioengineering and Nanotechnology (AIBN), which has allowed the two Institutes to develop common systems for IT delivery and backup.
- **Technical Services** (Dave Wheeldon) coordinates the delivery of workshop facilities and is responsible for the operation and safe management of QBI buildings and equipment.
- **Scientific Services** (Clare Seaman) coordinates the scientific support facilities of the Institute including safety, OGTR, AQIS, purchasing, induction, media and quality control.
- **Commercialisation** (Annita Nugent) coordinates the commercial activities of the Institute through UniQuest (The University of Queensland's Commercial unit) and the QBI Executive.

NEW BUILDING TAKES SHAPE

Work is almost complete on a $63 million seven-storey building, which will house state-of-the-art equipment and accommodate about 250 scientists. Scheduled for completion in August 2007, the building will enable the Institute to become one of the finest neuroscience facilities in the world. The Queensland Government has committed $20 million to this building with the remaining funding being provided by The University of Queensland ($23 million) and The Atlantic Philanthropies ($20 million).

Design team John Wardle Architects and Wilson Architects have modelled the new QBI facilities on a 'theatre for research' theme, with open interaction spaces aligned along the building's inside perimeter walls, while exposing the internal activity of research and exploration to the community. Features of the building include a dedicated research animal facility with purpose-designed behavioural testing facilities, aquaria, SPF facilities and surgeries. In addition, research spaces have been designed to maximise flexibility; spaces can be rapidly configured to support

▼ **Lab Safety Committee: (L–R)** Tim Butler, Amanda Hammond, Petra Sedlak, David Wheeldon, Clare Seaman

▼ **Finance Section: (L–R)** George Styles, Katherine Parsonage, Wade Ebeling

PEOPLE AND PUBLICATIONS

The links between levels have been designed to encourage interaction, with each floor having formal meeting rooms, as well as areas that can support informal, spontaneous discussion

molecular biology, tissue culture, electro-physiology and even robotics facilities.

To encourage scientific integration, dedicated core support facilities have been distributed throughout the building. Level seven is to provide an area where the Institute staff and visitors can come together – a 200-seat auditorium, a 40-seat seminar room for advanced computational imaging, as well as interaction and entertaining areas that can support as many as 300 people.

The links between levels have been designed to encourage interaction, with each floor having formal meeting rooms, as well as areas that can support informal, spontaneous discussion. QBI is looking forward to having the research groups together, all in one building.

QBI OPERATIONS AND SUPPORT STAFF

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Annita Nugent, *BSc, Dip Ed, Dip Law (LPAB), Registered Patent Attorney*
Charmaine Paiva, *BA*
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David Wheeldon
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Rowan Tweedale, *BSc*
Shani Doig, *BA Grad Dip Teach, Med*
Veronica Baldry
Wade Ebeling, *BA*

▼ **Laboratory Support Services**: **(L–R)** Alison Kelly, Lida Stjepcevic, Mary White, Jenette Zlamal, Clare Seaman

▼ **Technical Services**: **(L–R)** Dario Hogg, Trent Bell, Graham Bell, Peter Gordon, Adam Barry, Ken Edgeworth, David Wheeldon, Wade Rawlings

ACKNOWLEDGEMENT OF **SUPPORTERS**

Australian Cancer Research Foundation

QBI is proudly supported by the Australian Cancer Research Foundation

PETER GOODENOUGH LEGACY FOR **MND RESEARCH**

When QBI's new facilities are completed, a laboratory within the new complex will be named in honour of Peter Goodenough, a Cairns-based motor neuron disease (MND) sufferer who donated $3 million to QBI to enable further groundbreaking research into this debilitating disease.

Mr Goodenough, who died in December 2004, worked closely with the University's Development Office to ensure his personal wealth would be put to good use in the fight against MND. At the peak of his working life, Mr Goodenough owned and operated a mining engineering and equipment hire business at Awara in Papua New Guinea.

▲ Born in the United Kingdom, Peter Goodenough spent many years in Bougainville in the 1970s and 1980s.

▲ **(L–R)** Perry Cross, UQ Vice-Chancellor Professor John Hay, SpinalCure Australia CEO Bob Turner and QBI Director Professor Perry Bartlett at the inauguration of the Lisa Palmer Spinal Research Consortium.

LISA PALMER BEQUEST **BOOSTS SPINAL CORD RESEARCH**

A young quadriplegic woman's courageous life and premature death may lead eventually to a cure for people paralysed by spinal injury.

In October 2005, The University of Queensland accepted a bequest of $650,000 from the estate of 29-year-old Lisa Denise Palmer, who died of cancer in 2004 after living with a severe spinal cord injury. The grant from SpinalCure Australia for the Lisa Palmer Spinal Research Consortium will be headed by the Queensland Brain Institute.

Ms Palmer's bequest will fund research at QBI, the Queensland Institute of Medical Research and the University of Melbourne Centre for Neuroscience.

QBI Director Professor Perry Bartlett said the bequest would fund three years of basic scientific research, with part of the bequest being set aside for human clinical trials in the fourth year.

Paralysis caused by spinal injury affects about 18,000 people in this country and the average age of Australians when injured is nineteen.

▲ Mr Ross Maclean, founder of The Index Group of Companies, who sadly passed away in February 2005. Mr Maclean funded creation of a Fellowship to study motor neuron disease at the Queensland Brain Institute.

FAMILY COMPANY ESTABLISHES UQ FELLOWSHIP TO **FIGHT MOTOR NEURON DISEASE**

Before Ross Maclean (pictured) passed away in February 2005, the successful businessman decided he would do something to combat the debilitating disease he knew would finally end his life.

At 80 years of age, Mr Maclean and his family established a Fellowship dedicated to researching motor neuron disease (MND), a condition for which there is currently no adequate treatment or cure.

In 2004, Mr Maclean's company the Index Group underwrote fundraising of $100,000 for the first year and $50,000 for each of the next two years for the Ross Maclean Fellowship to study MND.

The Fellowship, awarded to Dr Robyn Wallace, was created after Mr Maclean met with QBI Director Professor Perry Bartlett.

Mr Maclean was diagnosed with MND in about 2000 after experiencing numbness in some of his limbs followed by a gradual deterioration in fine motor skills such as using keys, writing and turning on switches.

His son, Jeff, said his father had delayed telling his family so as not to unduly worry them. Mr Maclean senior and his wife, Daphne, have six grandchildren through Jeff and his older brother Craig, Deputy Principal of Bundaberg State High School.

When diagnosed with MND, Mr Maclean senior was Managing Director of the Index Group of Companies, one of Queensland's top 400 privately owned companies and long-time major sponsor of the Souths Rugby Union Club in Brisbane.

In fact, in 1976, Index was the first company to sponsor rugby union anywhere in Australia and Mr Maclean senior was the club's patron while Jeff played for the club in nearly 200 games in the 1970s and 1980s.

The Index Group's wide-ranging business interests include designing and manufacturing commercial water filtration equipment, and selling second-hand mining and quarrying equipment.

Jeff said the company would fundraise by approaching people for donations directly rather than organising any major events.

KOKODA TREKKERS RAISE FUNDS FOR MND RESEARCH AT QBI

A team trekking the famous Kokoda Track raised more than $48,000 for the Ross Maclean Fellowship in June 2006.

Eight days of climbing and descending the notoriously difficult Papua New Guinea highland path, often walking ten hours or more a day, was a huge test of endurance and something every Australian should do, Index Group Executive Director Jeff Maclean said.

"It was probably the hardest thing I've ever done, both physically and mentally," Jeff said.

Together with his son Hamish, brother Craig and brother-in-law Marcus Grealy, the team tackled some of the wildest jungle in PNG to raise funds for the Ross Maclean Fellowship – a scientific research fund established in 2004 by Jeff's late father – to study motor neuron disease at the Queensland Brain Institute.

Intense pre-trek training paid dividends for the team, as they all returned without incident or injury. While conditions on the Kokoda Track can vary from steamy tropical downpours to being quite cool at night, Jeff's team took it all in their stride – albeit a muddy one.

"During the first few days it rained non-stop for 36 hours," Jeff said.

"You're in mud, stepping between rocks and tree roots practically the whole time."

▲ Hamish and Jeff Maclean with Kokoda Track support crew in June 2006.

Jeff said the team was thrilled to be able to meet one of the original 'fuzzy wuzzy angels', the local villagers who played such an vital role in rescuing injured Australian soldiers from the frontline during WW2.

Part of the trek included hearing detailed accounts read from diaries of Australians who fought along the Kokoda Track, and learning about their wartime experiences.

WHAT IS MOTOR NEURON DISEASE?

MND, also known as Amyotrophic Lateral Sclerosis (ALS) or Maladie de Charcot, was first described by Charcot, a French neurologist, in the 1860s.

The condition affects more than 350,000 people worldwide, with a mortality rate of 100,000 people each year. In Australia, on average, one person dies of MND every day.

MND involves a deterioration of the nerve cells, or neurons, controlling key muscles including those in the trunk and limbs and those controlling speech, swallowing and breathing, while leaving the brain unaffected.

Symptoms of advanced MND include difficulty moving around and sleeping, breathlessness and fatigue, and stiff, swollen and cold limbs.

IN APPRECIATION

MAJOR DONORS/ SUPPORTERS

The Atlantic Philanthropies

The Queensland Government

The Australian Government

Peter William Goodenough

Lisa Palmer (Spinal Research Consortium, SpinalCure Australia)

The Index Group of Companies Pty Ltd

BEQUESTS AND DONATIONS OF MORE THAN $1000

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Alan Keet

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Big Rim Pty Ltd

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HOW TO SUPPORT THE QUEENSLAND BRAIN INSTITUTE

Researchers at the Queensland Brain Institute are dedicated to unlocking the mysteries of the many neurodegenerative diseases and mental health disorders, which currently account for a staggering 45 per cent of the burden of disease in Australia.

Research under way at QBI promises to lead to new treatments for disorders such as Alzheimer's disease, Parkinson's disease, stroke and depression.

As QBI relies on both government and non-government sources for the ongoing funding of its research programs, the Institute is grateful for the support and generosity of its benefactors, both private and corporate.

There are many ways in which to support QBI research efforts. Funds can be earmarked for research into specific neurodegenerative conditions or to help purchase scientific equipment.

Planned giving

Please speak to your solicitor or contact QBI for more information about how to include the Queensland Brain Institute in your Will.

Specific-purpose donations

QBI will be pleased to discuss the best way to ensure that your donation be applied to a particular area of research, or used in a way that helps to investigate the fundamental mechanisms that regulate brain function.

Gift of Assets or Property

Donors can elect to transfer assets or property to QBI in their Estate.

Research under way at QBI promises to lead to new treatments for disorders such as Alzheimer's disease, Parkinson's disease, stroke and depression.

Trust or Named Fund

Dedicated scientific research funds, such as the Ross Maclean Senior Research Fellowship for research into motor neuron disease, target specific areas of brain research. Please contact us to discuss which area of research you would like to support.

Acknowledgement

All donations to QBI are acknowledged by a letter and donations greater than $1000 will be published in the Institute's annual report.

Write a letter of support

By writing a letter to your local member of State/Federal parliament or the relevant Minister, outlining your support for neuroscience research, you can help encourage government funding. Please contact QBI communications should you need assistance in this regard.

Tax deductibility

Under current legislation, gifts to The University of Queensland – and QBI – are tax deductible.

To support QBI through gifts or donations, please write to:

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