The Florey
Advancing Brain Research

AuSCR
Australian Stroke Clinical Registry

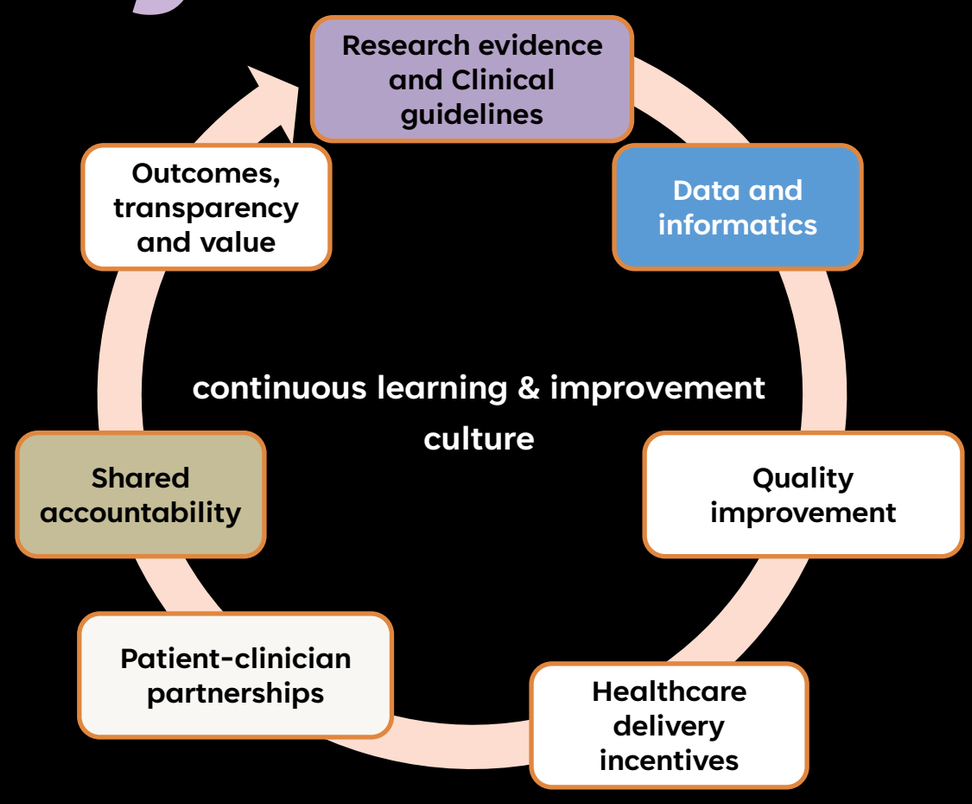
Australian Stroke Clinical Registry

About our research

The Australian Stroke Clinical Registry is a clinical quality registry to monitor and improve the quality of acute stroke care in Australia.

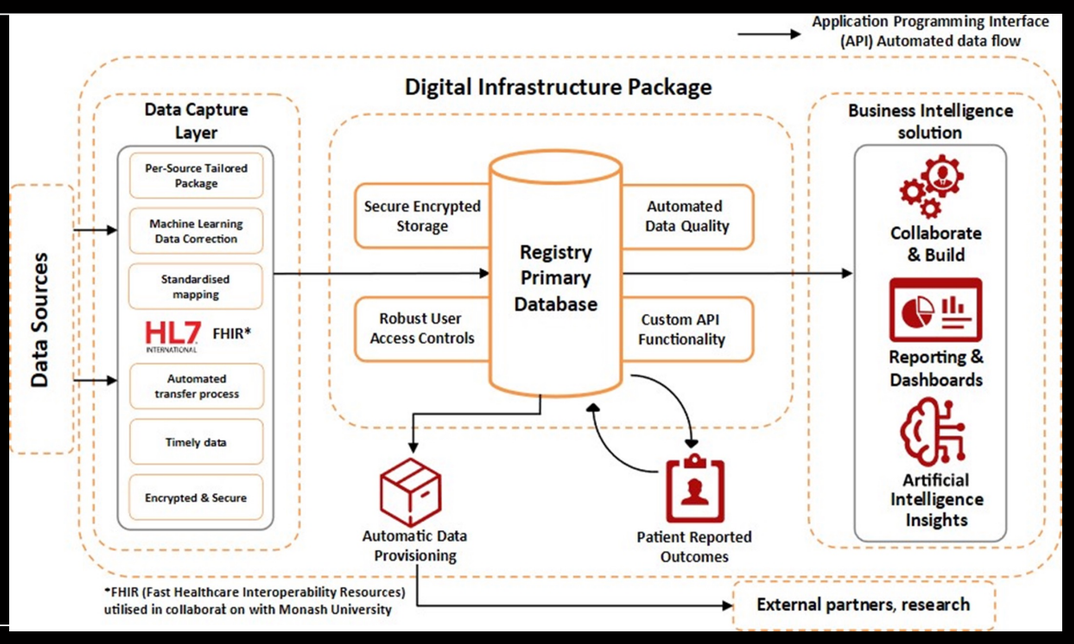
Sixty-four hospitals nationally contribute data on ~20,000 patients admitted to their hospitals with acute stroke per year. Patient reported outcome measures are collected 90-180 days following admission.

The AuSCR provides on-demand reports where hospitals can compare their performance on a range of key performance indicators to other hospitals and an achievable benchmark. Formal reports to hospital contributors and hospital CEOs are also provided.



The future

The AuSCR has recently received a Medical Research Future Fund grant to create Australia's first digital clinical quality registry platform. This project includes developing solutions for hospitals to automatically transfer data into the registry.



Projects available for 2024

- Stroke learning health systems – optimising use of data to support clinicians in providing best practice care
- Investigation of sex differences in stroke care
- Effectiveness of interactive dashboard implementation
- National stroke data dictionary mapping
- Interoperability status of hospitals in Victoria

Research interest key words

- Stroke, clinical quality registry
- Machine learning, artificial intelligence
- Interoperability with hospital electronic medical record systems

Looking for

- Students with an interest in health services research, digital health systems, artificial intelligence, machine learning, epidemiology, biomedical or nursing/allied health research.

AuSCR homepage

Florey AuSCR website

Contact information

Julie Morrison

AuSCR Program Manager

Julie.Morrison@florey.edu.au

The Florey
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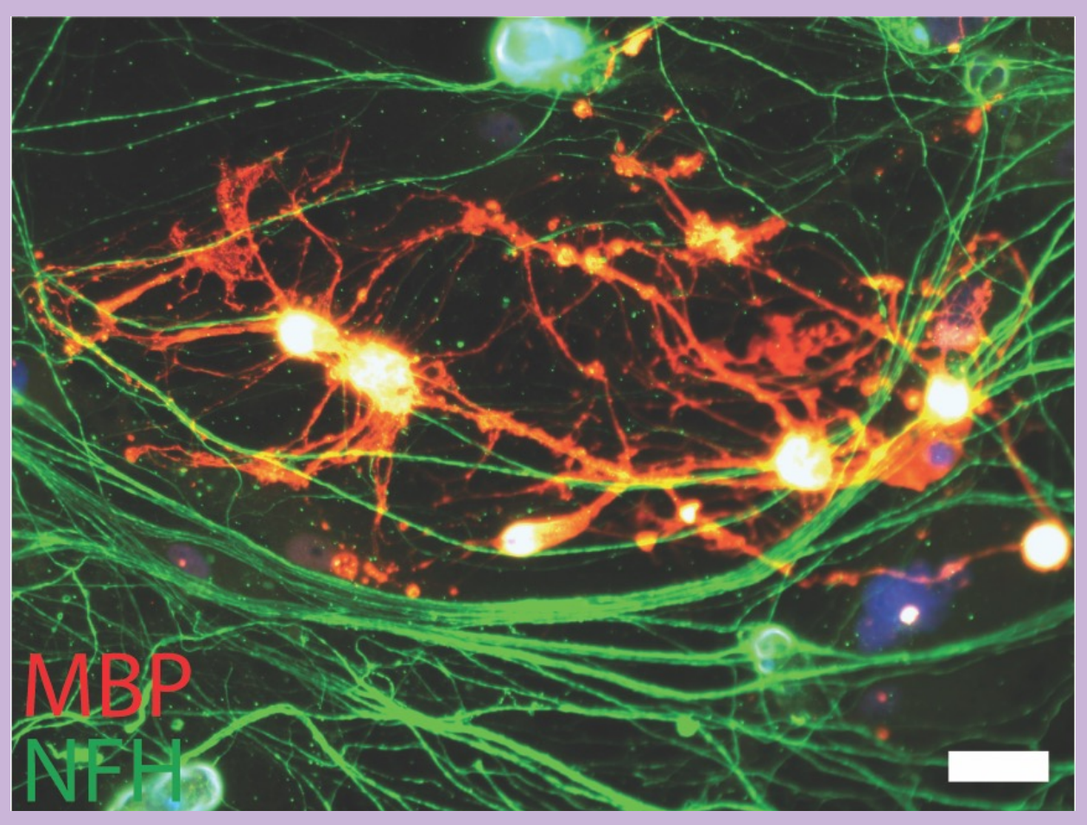
Multiple Sclerosis and Myelin Repair Group

About our research

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system (CNS), affecting over 2 million people worldwide. Current MS treatments do not prevent ongoing neural damage that leads to progressive disability. Our group is focused on developing new treatments that promote myelin repair to reduce neuronal damage in MS.

Our multidisciplinary team has expertise in myelin biology, genetics and neuroinflammation. We work collaboratively to investigate questions ranging from basic biology, through to translational research, developing novel therapeutic treatments for MS.



Research interest

- Multiple sclerosis
- MicroRNA
- Remyelination
- Neuroinflammation

Techniques

- Culture of primary cells and immortalised cell lines
- Human stem cell and organoid culture
- Pre-clinical models of MS
- Transcriptomics

Titles of projects available for 2024

- How are the brain's immune cells regulated?
- A brain in a dish
- Microglia in myelination
- Developing and testing PEGylated GAS6 as a potential remyelinative therapy for multiple sclerosis

Looking for

- Honours student
- Master student

Contact information

Michele Binder (Group Head)

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Sarrabeth Stone

sarrabeth.stone@florey.edu.au

The Florey
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Digestive Physiology and Nutrition Group

About our research

Our group focuses on digestive physiology and nutrition, including the gut-brain axis. We use animal models of digestive diseases, including inflammatory bowel disease.

@TheFurnessLab

Projects Available

- **Gut-brain communication: How the stomach and brain communicate**

The stomach is the portal to the digestive tract. The stomach tells the brain about its state: How full it is, what is the nature of its contents, are any toxins present. The brain reacts by eliciting feelings of hunger, satiety, fullness, nausea or wellness. In turn, the brain tells the stomach what to do, after integrating information coming from the stomach and other information, including the sight, smell and proximity of food. Miscommunications can lead to maldigestion, severe pain and/or discomfort in patients. In this project you will investigate this two-way communication that is essential to a healthy life.

- **A stem cell therapy for Hirschsprung Disease**

Hirschsprung disease (HSCR) is a congenital enteric neuropathy characterised by the lack of enteric neurons in the distal bowel, which results in a loss of propulsive motility and life-threatening constipation. Without surgical removal of the defective bowel, the infant dies. Current surgical intervention, while life-saving, frequently results in chronic, long-term complications, including constipation, fecal soiling, and associated psychosocial problems. Consequently, alternative treatments are needed.
In this project you will participate in the surgical rescue of Hirschsprung rats, you will be involved in the development of stem cell therapies, and you will evaluate recolonization using structural and functional methods.

- **Neural control of inflammation: Therapies for inflammatory disease**

Inflammatory bowel disease is common, chronic and debilitating. A major form of IBD, Crohn's Disease, almost always recurs, even after the affected region has been surgically removed. Patients and their families are desperate for new, effective treatments that are safe and have limited side effects. This project represents a dramatic paradigm shift resulting from our discovery of sympathetic nerve involvement.
We are systematically investigating the pathways of neuroimmune interactions in the intestine, including vagal, sympathetic and enteric nervous system pathways. We are closely comparing neuro-immune changes that are associated with active inflammation and remission both in human and in an animal model.
The project involves a team of neuroscientists, physiologists, clinicians and bioengineers working closely together, with whom you will work.

- **Novel heteromeric receptors: Ghrelin receptors and dopamine receptors working together**

Ghrelin is a naturally occurring hormone with effects in the central nervous system (CNS). We discovered that ghrelin is a powerful CNS-acting stimulant of defecation in animal models and humans. A striking conclusion from our discoveries is that the strong stimulation of defecation by ghrelin agonists is independent of ghrelin, which we discovered to be absent from the CNS. Our data indicate that the physiological role of the ghrelin receptor, GHSR, is to reverse the actions of dopamine at the DR2 receptor. In this project, you will be investigating how ghrelin and dopamine receptor agonists interact in native and isolated cells.

Looking for: Honours students - Master students - PhD students

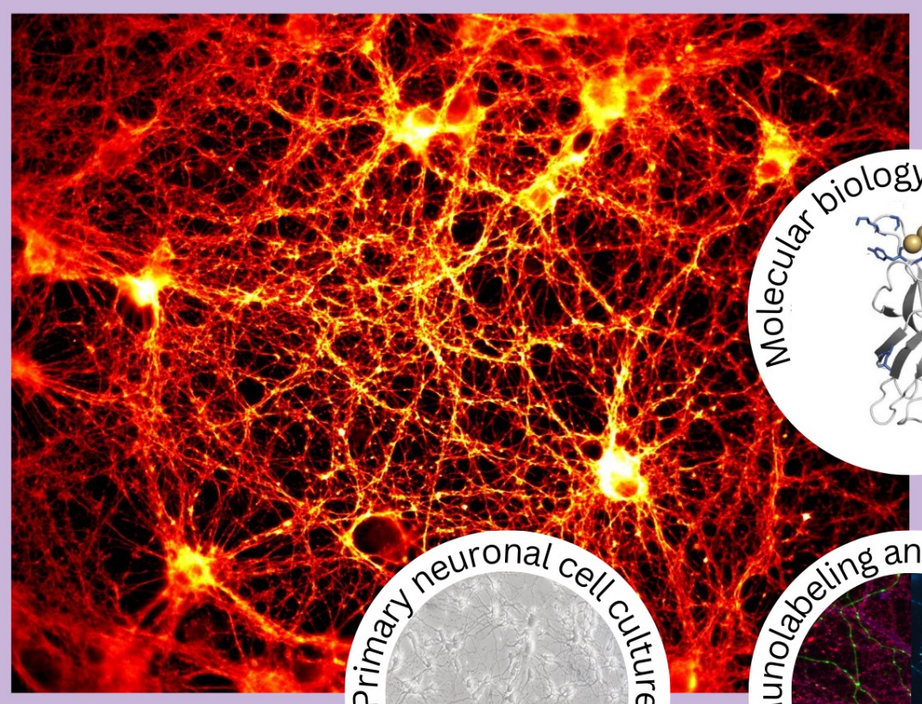
Contact information

Professor John Furness: john.furness@florey.edu.au

Ms. Madeleine Di Natale: madeleine.dinatale@florey.edu.au

The Florey
Advancing Brain Research

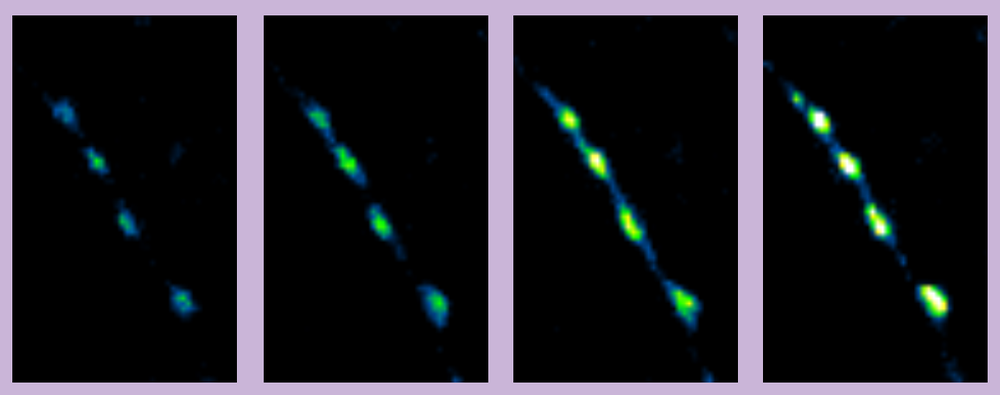
The Gordon Presynaptic Physiology Lab



The reliable and efficient release of neurotransmitters is essential to neuronal communication. Tight regulation of this process is achieved by an intricate and complex array of protein machinery at synapses.

Malfunction of this machinery results in defective neurotransmission and is implicated in the pathogenesis of a variety of neurodevelopmental and neurodegenerative disorders.

Our lab focuses on exploring the proteins that regulate synaptic function, and how dysfunction of these proteins (eg. through genetic variants) lead to a spectrum of distinct neurological disorders.



Research interest key words

- Neurodevelopmental disorders – Intellectual disability, Epilepsy, Autism Spectrum Disorder
- Neurodegenerative disease – Parkinson's Disease
- Genetic variants
- Synapses, neurotransmission, protein function

Techniques

- Live-cell fluorescence imaging
- Immunocytochemistry
- Primary neuronal cell culture
- Biochemistry and molecular biology – cloning, site-directed mutagenesis, proteomics

Titles of projects available for 2024

- Investigate how mutations in SYT1 affect the synaptic vesicle cycle, and whether these effects are treatable
- Investigate how alpha synuclein regulates the synaptic vesicle cycle and neurotransmitter release
- Investigate how phosphorylation controls the function of alpha synuclein at nerve terminals

Looking for

- PhD, Masters, & Honours students

Contact information

Dr Sarah Gordon

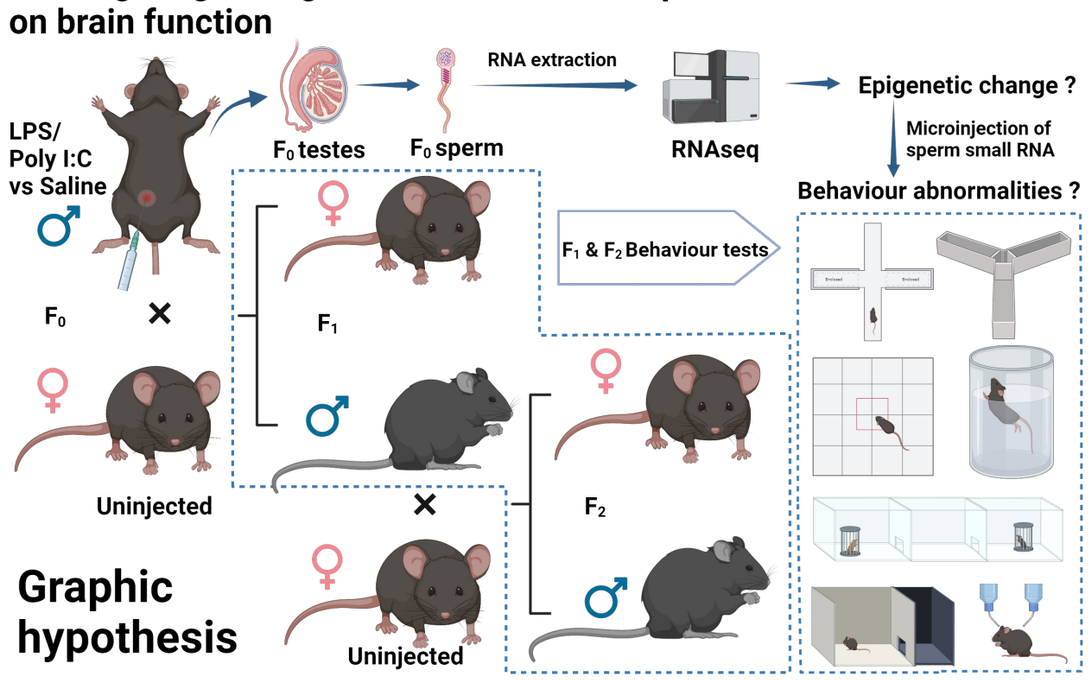
Lab Head

sarah.gordon@florey.edu.au

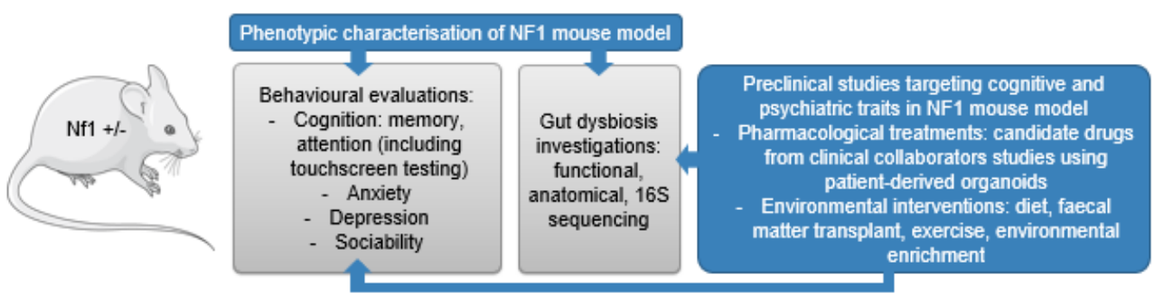
The Florey
Advancing Brain Research

Epigenetics & Neural Plasticity Lab

Investigating multigenerational effects of paternal immune activation on brain function



Neurofibromatosis Type I: targeting cognitive and psychiatric symptoms using a heterozygous mouse model

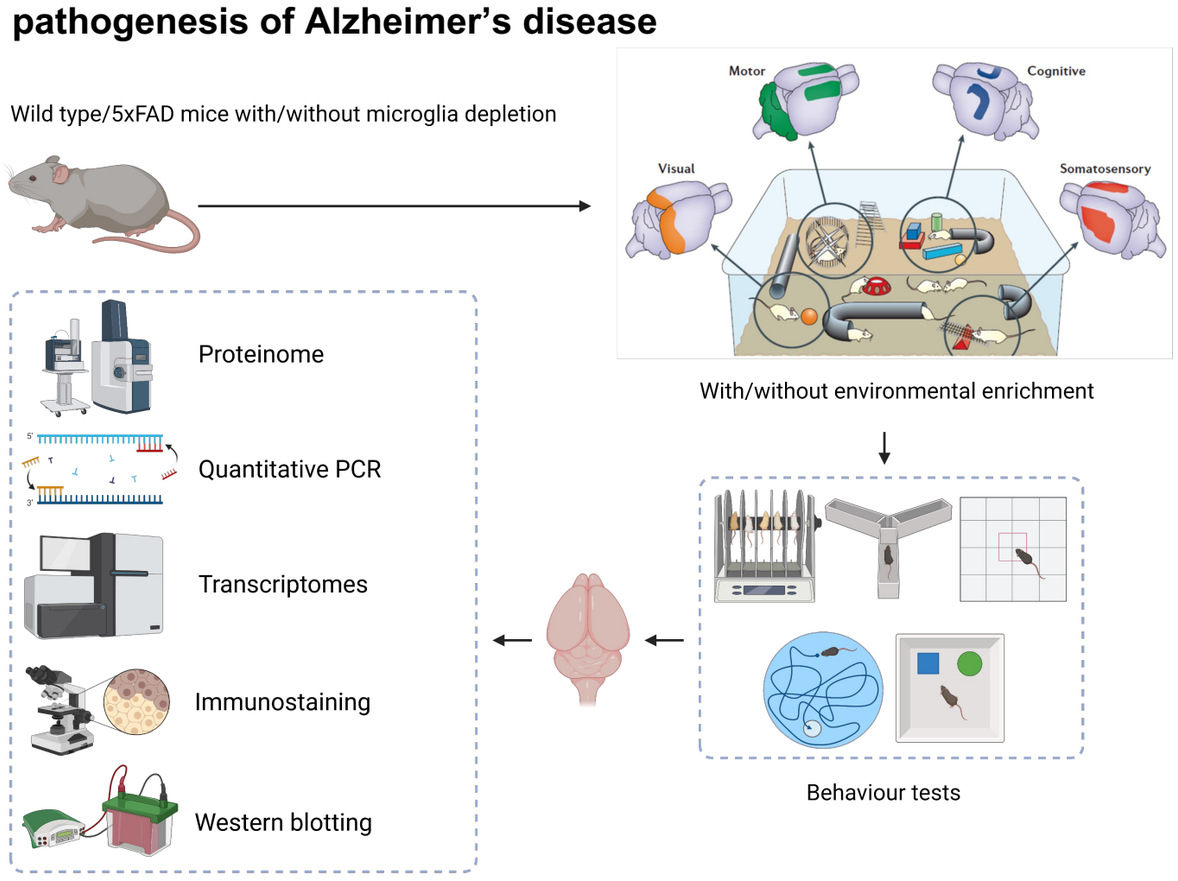


Methods:
Rodent behavioural tests and investigation of molecular mechanisms

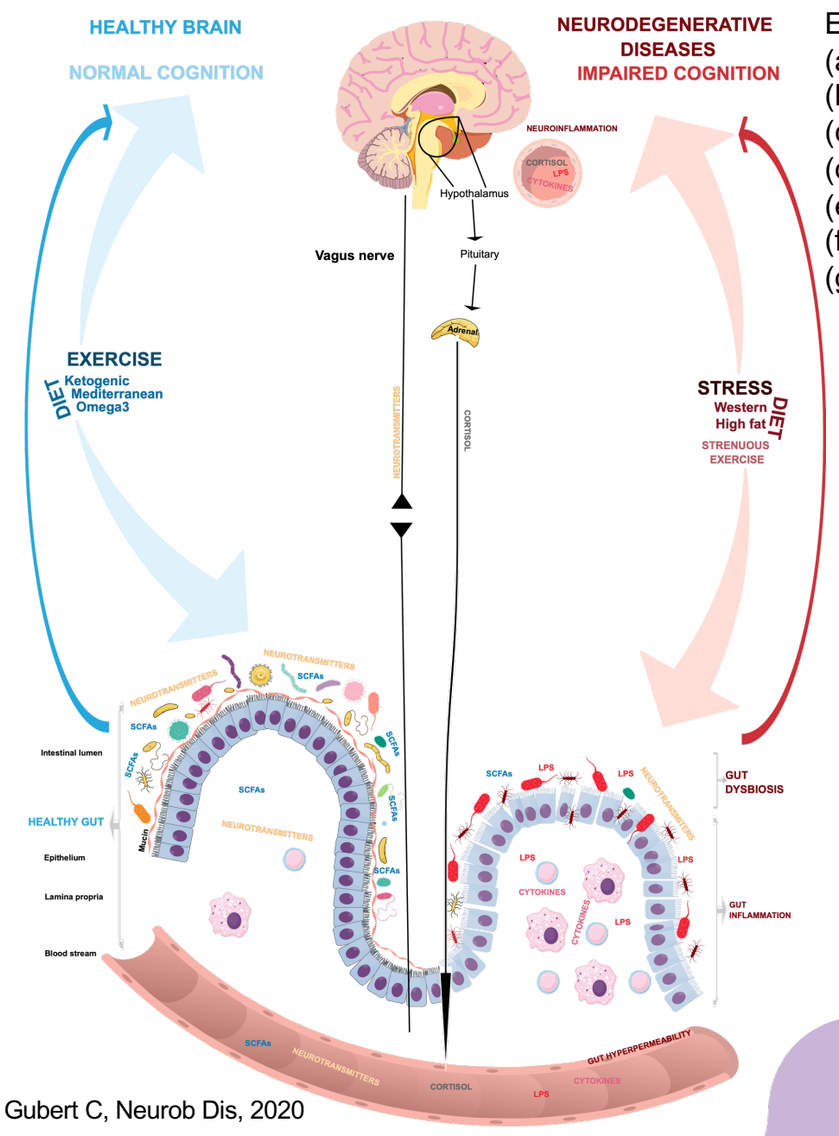
Spatial memory	Working / Short-term memory - novel object, novel location test, y-maze and t-maze, Trial-unique non-match to place test (touchscreen) Long-term - water maze, paired associated learning (touchscreen)
Executive function	Reversal learning (watermaze, touchscreen)
Attention	5-choice serial reaction task, continuous performance test, mPosner task (touchscreen)
Language	Ultrasonic vocalization analysis (deep-learning detection/clustering)
Motor behaviour	Rotarod, open field, pole test, Erasmus ladder
Depression	Porsolt swim test, novelty-suppressed feeding, saccharine preference
Psychosis-like behaviour	Prepulse inhibition (PPI) of acoustic startle, hyperactivity (spontaneous or drug-induced)
Social behaviour	Maternal care, social interaction test, conditioned social reward, social interaction between multiple mice using RFID technology, sexual behaviour test, resident intruder test (aggression), grooming

<u>Other models:</u> Exercise (wheel running), environmental enrichment, etc.
<u>Bioinformatics</u>: Nanopore sequencing (DNA modifications including methylation), RNA seq (small noncoding RNAs, long noncoding RNAs, mRNA), Proteomics
<u>Molecular Biology:</u> Western Blot, qRT-PCR, immunohistochemistry

The role of gene-environment interactions and microglia in the pathogenesis of Alzheimer's disease



Microbiota-gut-brain axis in brain disorders



Experimental methods:
(a) fecal microbiota transplant
(b) antibiotic cocktail
(c) dietary interventions
(d) environmental interventions
(e) stress
(f) target gut inflammation
(g) vagotomy

Gubert C, Neurob Dis, 2020

Investigating pathophysiological mechanisms and therapeutic targets in mouse models of gene-environment interactions, neuropsychiatric and neurodegenerative disorders

Contact information

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Dr. Huan Liao	huan.liao@florey.edu.au
Dr. Sonali Reisinger	sonali.reisinger@florey.edu.au

The Florey
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Epigenetics and Neural Plasticity Group

About our research

Our group investigates gene-environment interactions and experience-dependent plasticity in the healthy and diseased brain. We explore how genetic and environmental factors combine to influence predisposition to specific brain disorders, both within and between generations.

Research interest

- Huntington’s disease and associated psychiatric symptoms and dementia
- Autism, schizophrenia, depression and anxiety disorders
- Neurofibromatosis (NF1) and associated autism, ADHD and learning difficulties
- Brain plasticity in health and disease
- Genetic and environmental factors causing cognitive and affective disorders
- Epigenetics within and between generations
- Effects of stress, exercise, cognitive stimulation, diet and infection on the brain
- The gut microbiome and microbiota-gut-brain axis in health and disease

Titles of projects available for 2024

- Experience-dependent plasticity modulating cognitive deficits in schizophrenia
- Gene-environment interactions modulating dementia and depression in a tandem repeat disorder
- Identifying and manipulating the neural circuits of decision-making
- The microbiota-gut-brain axis and microbiome modulation in pre-clinical models of psychiatric disorders
- Transgenerational epigenetic inheritance modulating brain function, behaviour and cognition
- The role of gene-environment interactions and microglia in the pathogenesis of Alzheimer's disease

Looking for

- Honours students
- Master students

Contact information

Professor Anthony Hannan
Group Head
anthony.hannan@florey.edu.au

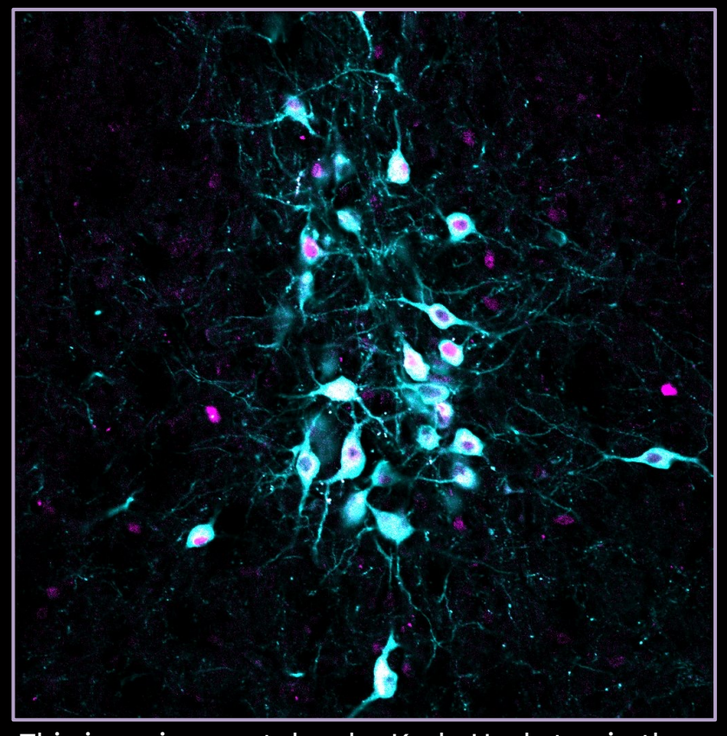
The Florey
Advancing Brain Research

Addiction Neuroscience Group

About our research

Over 100 million people globally have an alcohol or substance use disorder, with ~1 in 20 Australians having such an addiction. ~32 million disability-adjusted life years were attributable to drug use in 2016. Troublingly, rates of relapse remain high, with current treatments having limited efficacy.

Our broad aims are to:
- Develop translationally relevant preclinical models, that more accurately reflect the human condition.
- Elucidate the underlying neurobiology of substance use and misuse behaviours.
- To identify and validate novel targets for the treatment of substance use disorders



This is an image, taken by Kade Huckstep in the lab, of the Edinger Westphal nucleus, showing all the cells expressing the neuropeptide CART (cyan), and ones that were active during our behaviour of interest (magenta)

Research interest

- Addiction
- Drug-seeking
- Sex differences
- Alcohol
- Reward
- Motivated behaviour
- Neural mechanisms and circuitry
- Preclinical models
- Novel therapeutics
- Neuropeptides and neurotransmitters

Techniques

- *Behavioural paradigms*, e.g. drug-related behaviours, anxiety, locomotor, social behaviour.
- *Stereotaxic surgery*, e.g. viral injections, microinjection cannula and fiber optic implantation.
- *Tissue staining*, e.g. immunohistochemistry, in-situ hybridisation.
- *And many more,* e.g. electrophysiology, qPCR, RNA-Seq, microscopy.

Titles of projects available for 2024

- A novel treatment for alcohol and nicotine addiction.
- Muscarinic receptors and alcohol seeking.
- Sex differences modulating anxiety and binge-drinking behaviours.
- The role of appetite regulating hormones in alcohol intake.

Looking for

- Honours students
- Masters students
- PhD students

Contact information

Please contact Prof. Andrew Lawrence for any inquiries:

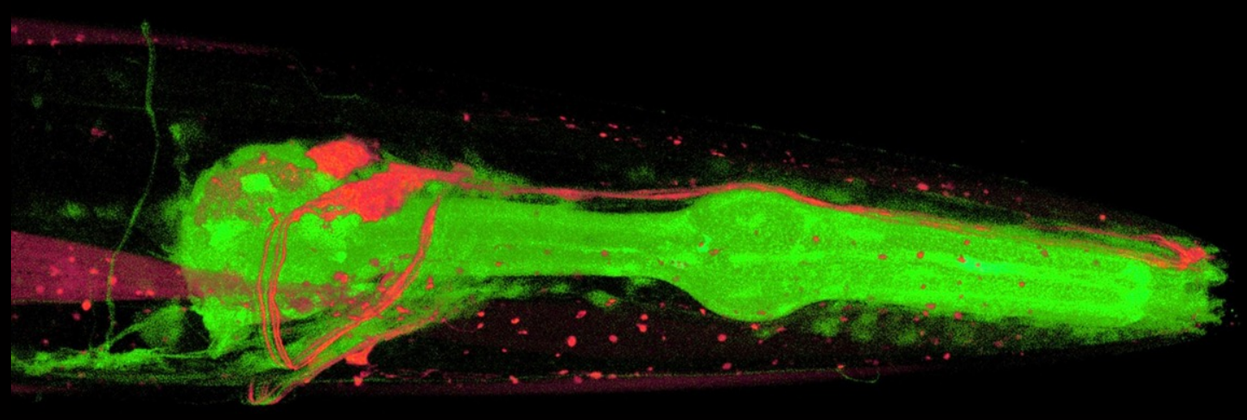
andrew.lawrence@florey.edu.au

The Florey
Advancing Brain Research

Molecular Gerontology Group

About our research

Ageing is universal in multicellular organisms. How ageing and lifespan can be modulated is an area of significant scientific interest. Our group explores the mystery of human ageing, with particular focus on the brain changes over lifetime.



Research interest key words

- Parkinson's
- Dopamine, iron and ferritin homeostasis
- Neurodegeneration

Techniques

- *C. elegans* genetics
- *Genetic engineering*
- *In vivo* imaging
- Optogenetics

Titles of projects available for 2024

- Iron and biological ageing
- Rapid animal models of Neurodegeneration
- Support cells and dopaminergic neurons

Looking for

- PhD students
- Master students

Contact information

A/Prof Gawain McColl

Group Head

gawain.mccoll@florey.edu.au

The Florey
Advancing Brain Research

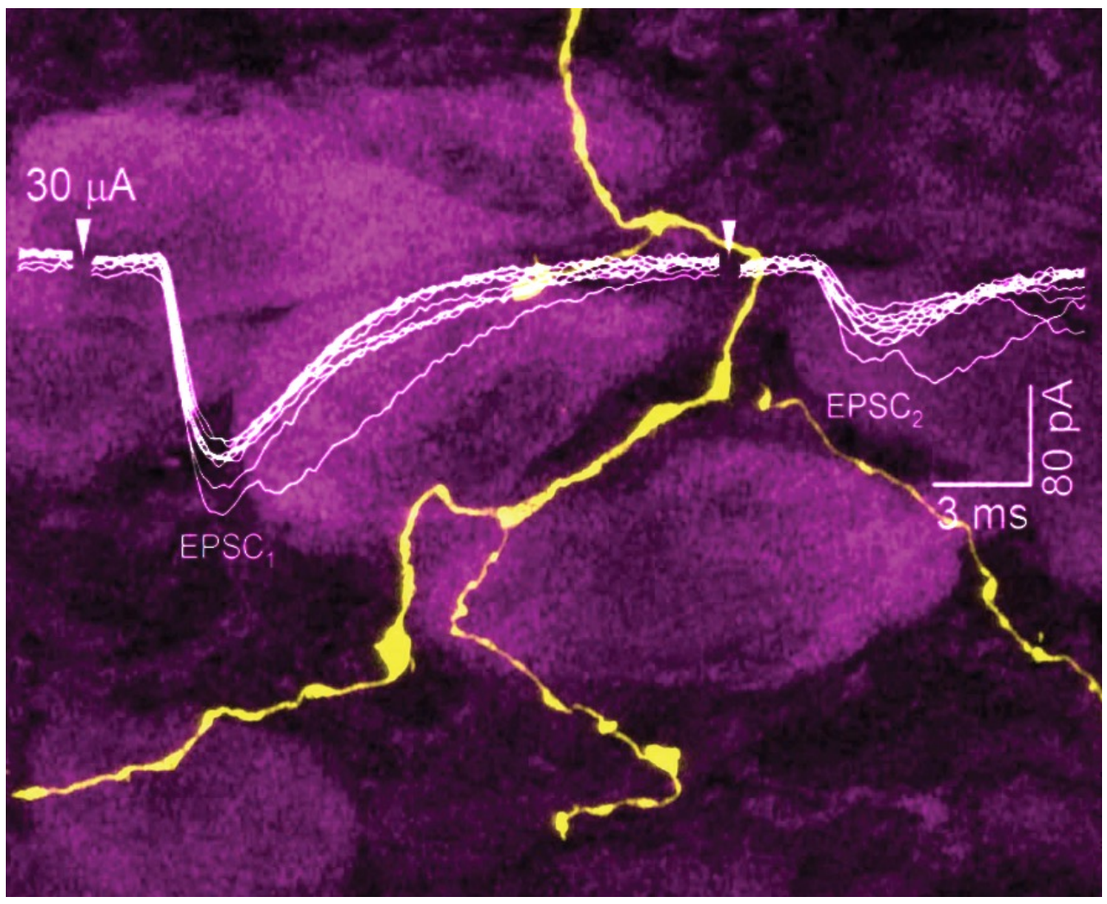
Viscerosensory Group

About our research

We study the basic neurophysiology underpinning integration of sensory information within the brain.

Our focus of study is the vagal sensory signalling from visceral organs including those of the cardiovascular, respiratory, and gastrointestinal systems.

Knowledge about how the brain and internal organs co-ordinate is relevant to several disease states, autonomic related; hypertension and obesity and mental health; stress and anxiety.



Research interest key words

- Viscerosensory signal processing
- Metabolic diseases
- Autonomic reflexes
- Interoception

Techniques

- Patch Clamp Electrophysiology
- Ca^{++} Imaging
- Behavioural assays
- Optogenetics
- Chemogenetics

Titles of projects available for 2024

- Optogenetic activation of vagal afferents to decode viscerosensory signal processing within the brain
- Do vagal afferents synapse at parasympathetic motor neurons within the brainstem?
- Mapping and defining the vagal viscerosensory information to the upper spinal cord
- Determining the vagal contribution to appetitive drive.

Looking for

- Honours students
- Master students
- PhD students

Contact information

Dr Stuart McDougall
Group Head
stuart.mcdougall@florey.edu.au

The Florey
Advancing Brain Research

Florey Microscopy Facility

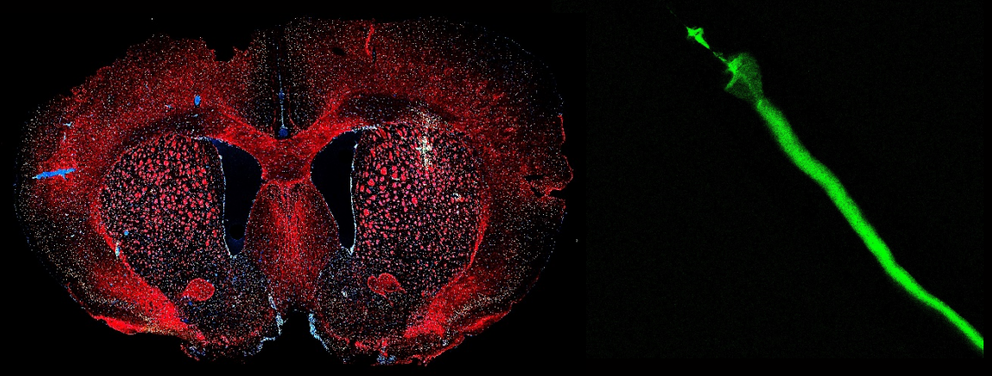
Manager: Carolina Chavez, PhD

Support Officer: Alita Soch, PhD

Introduction

The Microscopy Facility is located on level 4 KMB building. The facility houses multiple confocal and widefield instruments used for imaging a variety of samples.

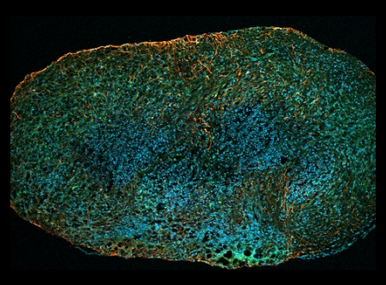
The Microscopy Facility also has analysis workstations on level 5 to analyse imaging data sets.

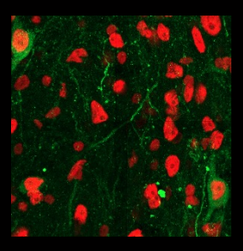


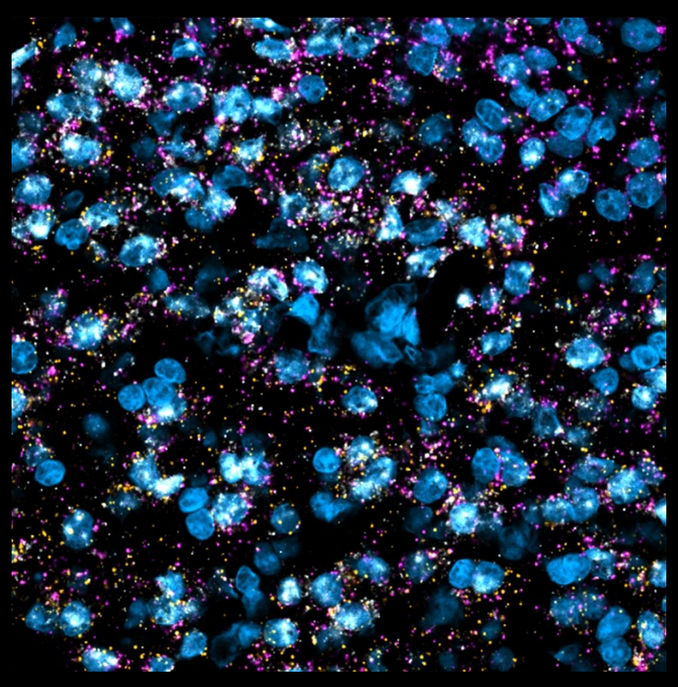
Services and Support

The dedicated staff provide:

- Instrument training & post-training support
- Tailored advice on imaging techniques, sample preparation & post-acquisition analysis
- Assistance with imaging-related manuscript preparation







Imaging Capabilities

Instruments:

- Confocal microscopes
- Spinning disk confocal microscope
- Fluorescent and widefield microscopes

Applications:

- Super-resolution (Airyscan/DeepSIM)
- Z-stack
- Tiled imaging
- Spectral imaging
- 5 channel imaging
- Brightfield imaging
- Fluorescent imaging
- High-speed live imaging

Software capabilities

Stereo Investigator

- Quantifying cell numbers

Neurolucida

- Neuronal structure analysis and tracing

Imaris

- Image processing, 3D rendering, animation, segmentation

Huygens Deconvolution

- Contrast enhancement, resolution improvement

Contact information

mbc-microscopy@florey.edu.au

The Florey
Advancing Brain Research

Neural Circuits and Behaviour Group

About our research

One of the most challenging but fascinating questions in neuroscience is the neural basis of decision-making.

We recently showed that a neural pathway between cortex and thalamus propagates learned perceptual information, which is crucial for mice to perform whisker-based decisions (Mo et al., 2023, PMID: 37034798).

These and other pathways are manipulated and monitored to further understand decision-making in the healthy and anxious state.

Research interest key words

- Anxiety-related disorders
- Transthalamic pathways
- Decision-making
- Calcium imaging
- Optogenetics

Techniques

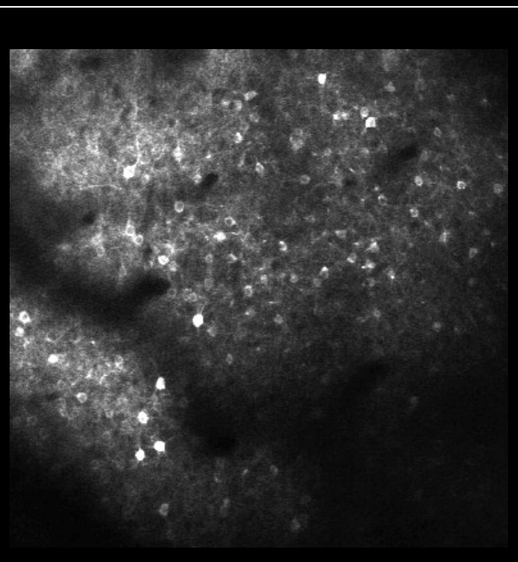
- Head-fixed and freely-moving decision tasks
- Optogenetics to control neural circuits
- Calcium imaging to monitor neural activity
- Rabies-based trans-synaptic circuit tracing

Titles of projects available for 2024

- Identifying and manipulating the neural circuits of decision-making
- Ameliorating decision anxiety in a mouse model

Looking for

- Honours students
- Master students
- PhD students



Contact information

Dr Christina Mo

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The Florey
Advancing Brain Research

Antibody Therapeutics Laboratory

About our research

One of the greatest challenges for treating brain diseases, is the inability of most drugs to effectively enter the brain. This includes monoclonal antibodies, highly effective therapeutic molecules used to treat a number of diseases. Furthermore, monoclonal antibodies are unable to transverse the neuronal plasma membrane to target intracellular antigens. To overcome the challenges of conventional antibody therapeutics, our lab has a strong focus on delivering antibodies as nucleic acids (cDNA and mRNA) in combination with synthetic and biological nanoparticles to enhance brain delivery and specifically target intraneuronal antigens. Our novel antibodies are tested in in vitro cell culture assays as well as in transgenic mouse models of human brain diseases.

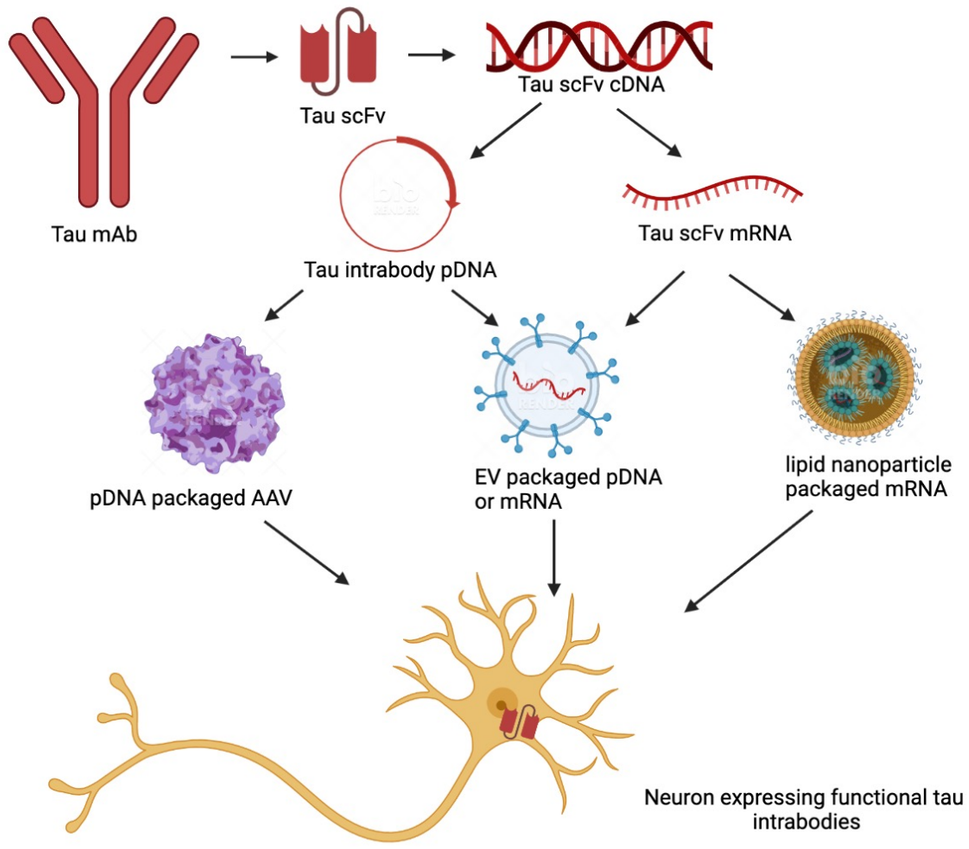

Figure. Schematic overview of our projects

Research interest key words

- Antibody therapeutics
- Alzheimer's disease
- Dementia
- Pre-clinical studies

Techniques

- Molecular biology (in vitro transcription, viral vector cloning)
- Biochemistry (western blotting, ELISA, protein expression and purification)
- Histology (tissue sectioning, immunofluorescence, immunohistochemistry)
- In vivo (mouse surgery, i.v and i.p injections, dissections & behaviour)

Titles of projects available for 2024

- Creating vectorized antibody therapeutics for enhanced brain targeting in Alzheimer's disease
- Extracellular vesicles as mRNA therapeutic delivery vehicles

Looking for

- Students with a BSc majoring in biochemistry, neuroscience or pharmacology
- Students with a passion for research

Contact information

Dr Rebecca Nisbet

Group Head

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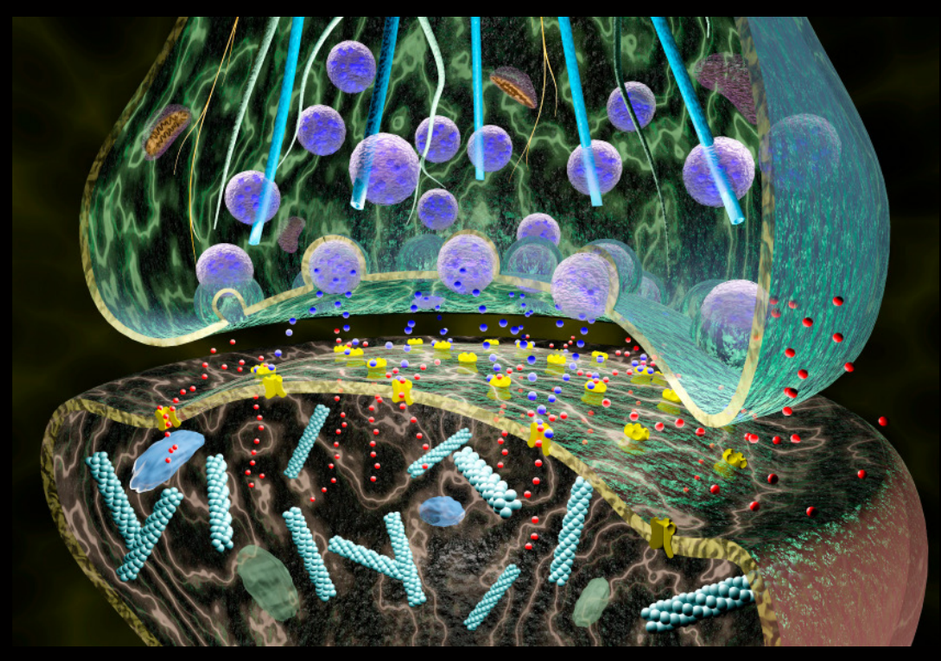
The Florey
Advancing Brain Research

Synapse Biology & Cognition Laboratory

About our research

Our work aims to uncover the neural basis of complex behavior and cognition, with a specific focus on the critical role the molecular machinery at synapses play in regulating brain connectivity required for complex cognition and higher order processing. We investigate these processes in healthy brains and in mouse models for mental disorders where these processes go awry. Bridging the gap between preclinical and clinical cognitive testing, we take a translation focused approach using touchscreen-based tests, an innovative tool for dissecting distinct cognitive domains in rodents that is highly analogous to cognitive assessment of clinical populations. We combine detailed behavioural analysis with advanced in vivo imaging techniques to measure real time neural activity changes during behaviour. Additionally, we explore treatment strategies to restore cognitive and neural deficits.

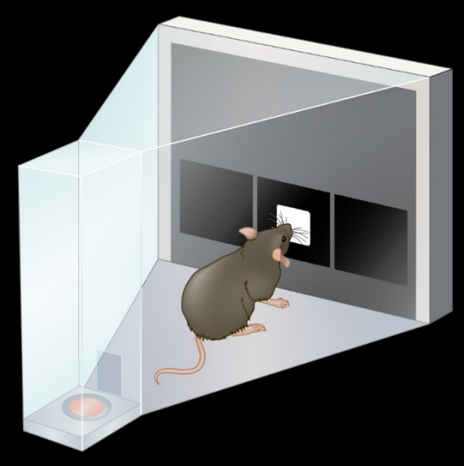


Research interest key words

- Synapses
- Cognition
- Schizophrenia
- Depression
- Autism Spectrum Disorders

Techniques

- Mouse models
- Rodent cognitive touchscreen testing
- Fiber photometry
- Miniscope cellular imaging
- In vivo pharmacology
- Optogenetics
- Deep-learning to measure behaviour



Projects available:

- Excitatory-inhibitory imbalance in neural networks regulating motivated behaviour

- Measuring disrupted neuromodulator signaling underlying maladaptive cognitive behaviour in neurodevelopmental psychiatric disorders

- Elucidating the molecular drivers underlying schizophrenia

- Deep-learning based tracking of behaviour in preclinical models for mental illness

Looking for

- PhD students
- Master students
- Honours students

Contact information

Associate Professor Jess Nithianantharajah

Group Head

jess.n@florey.edu.au

The Florey
Advancing Brain Research

PALMER LABORATORY

Professor Lucy Palmer
lucy.palmer@florey.edu.au
palmerlaboratory.com

Neural Networks Lab

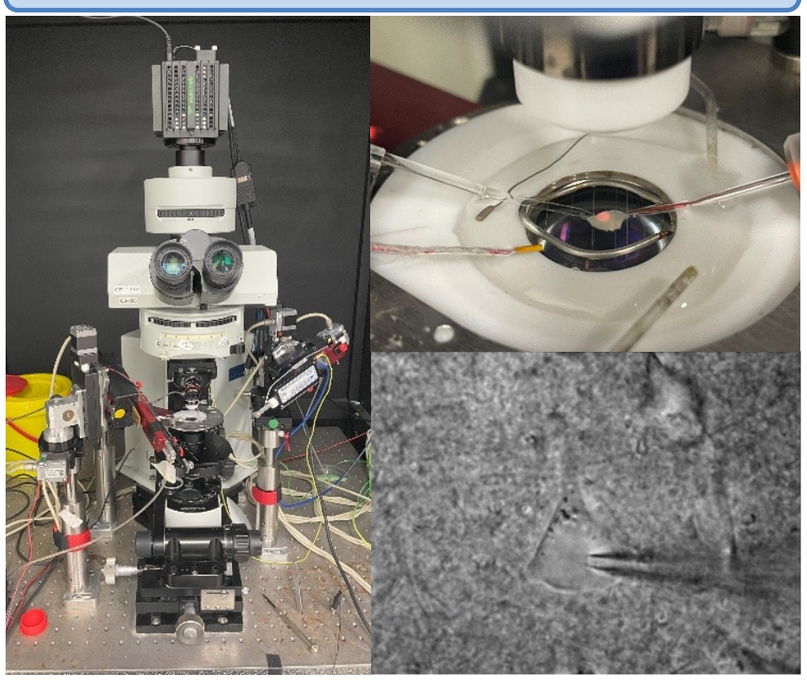
Professor Lucy Palmer

How does the brain work?

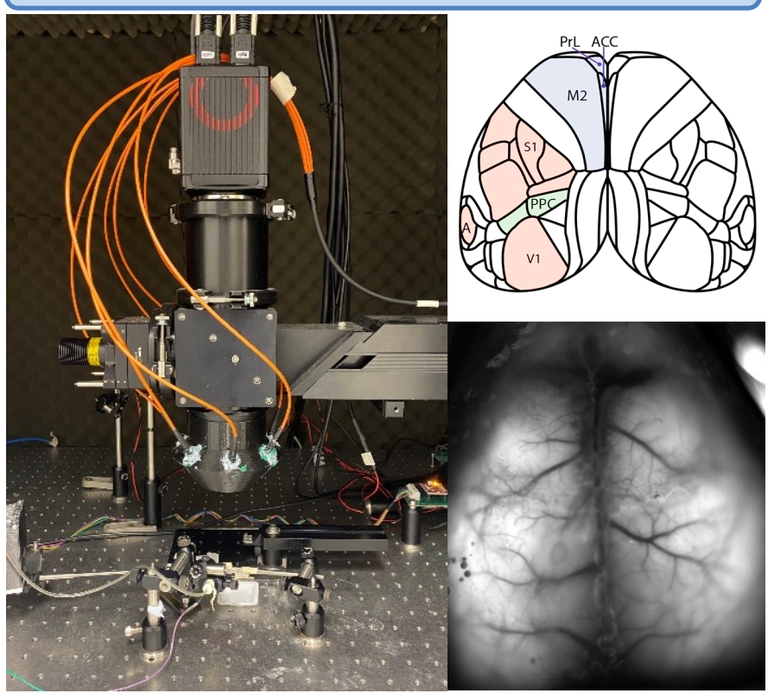
Looking for

- Honours students
- Master's students
- PhD candidates

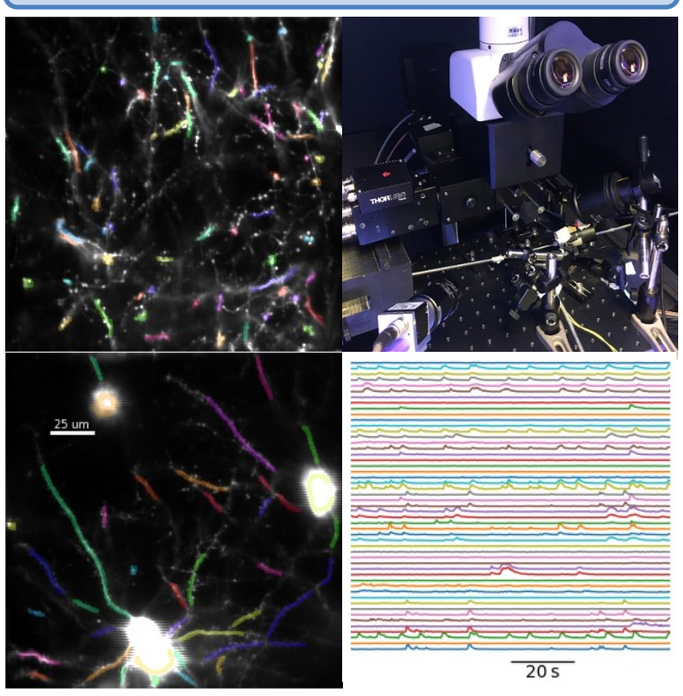
In-vitro and *In-vivo* Patching



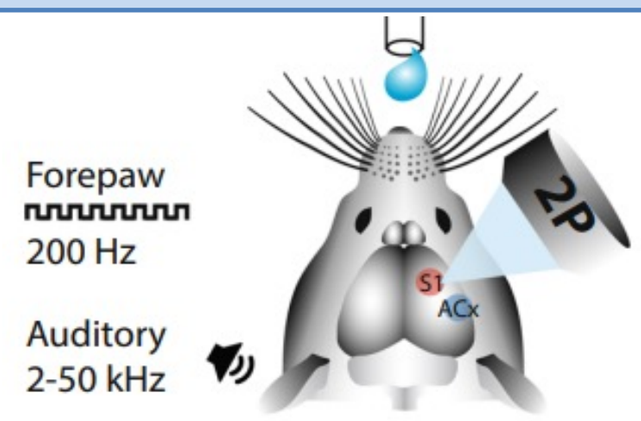
Widefield Calcium Imaging



Two-Photon Calcium Imaging



Behaviour and Neural Recordings



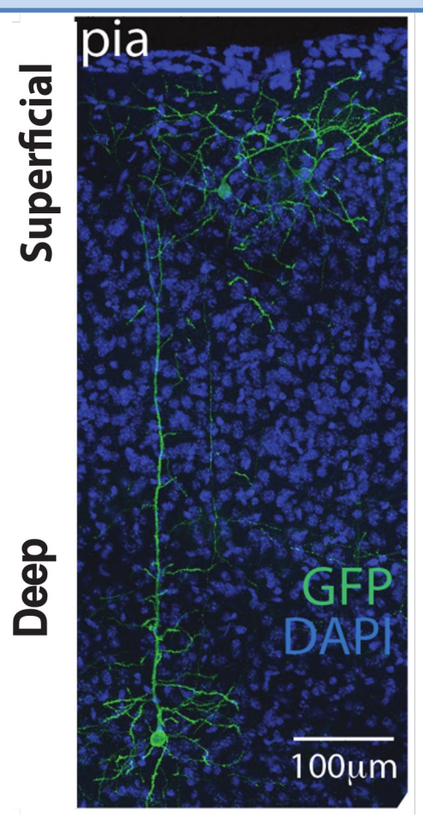
Tactile / AudTac-trial (Go)

lick = Reward	Hit
no lick	Miss

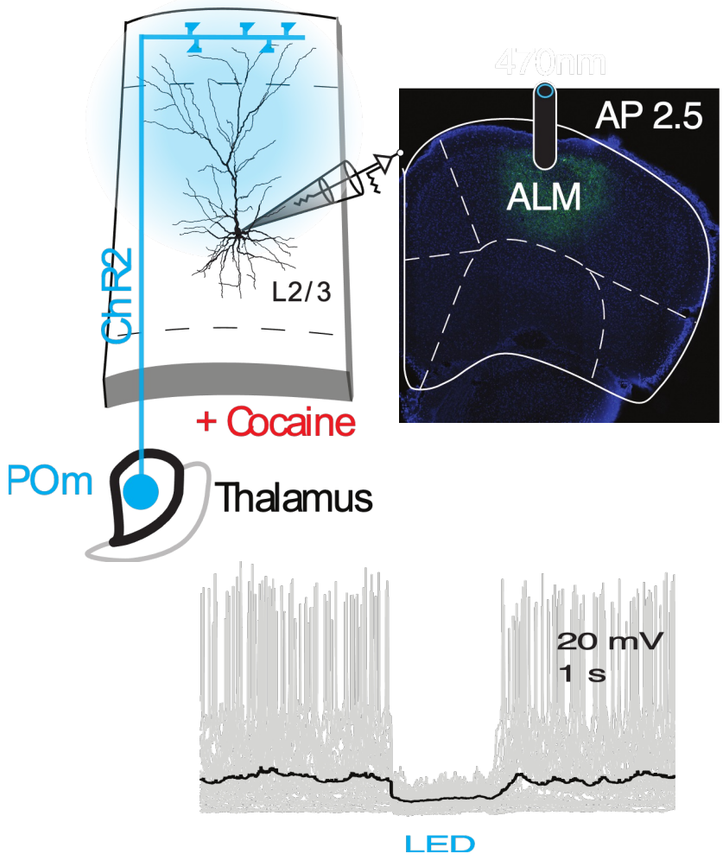
Aud-trial (NoGo)

lick = Timeout	FA
no lick	CR

Learning, Memory and Engrams



Optogenetics and Chemogenetics



Research themes

- Neural mechanisms driving memory
- Changes in neural encoding during learning
- How neural activity drives brain cancer proliferation
- Neural basis of behaviour

And more...

- Computation and modelling
- Tissue expansion
- Brain tumours
- Neuromodulation including psilocybin & cocaine

The Florey
Advancing Brain Research

Molecular Epidemiology & Bioinformatics PhD Scholarships available $34,400 p.a. (indexed) for 3.5 years

About our research

The Neuroepidemiology Group focuses on research into conditions affecting the brain and spinal cord, with a particular interest in autism spectrum disorder, ADHD, and multiple sclerosis. Our goal is to use population-based study data to gain a better understanding of these conditions, and particularly to identify potent points of intervention to reduce their risk and progression.

Research interest key words

- Autism
- Attention deficit/hyperactivity disorder
- Multiple sclerosis
- Epidemiology

Techniques

- Longitudinal cohort study
- Causal inference
- Causal mediation analysis

Titles of projects available for 2024

- Exploration of the direct and indirect mechanisms of Epstein-Barr virus on the risk and progression of multiple sclerosis
- Application of bioinformatic methodologies to tease out the genetic, epigenetic, and environmental mechanisms of EBV's effects on multiple sclerosis

Looking for

- Persons with experience in longitudinal epidemiological studies, ideally with exposure to complex data structures
- Persons with previous exposure to and use of varied and complementary measures of exposure

Contact information

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Dr Steve Simpson-Yap

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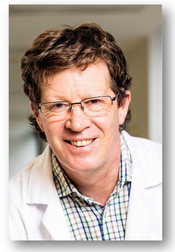
Neurophysiology of Excitable Networks Laboratory

The Florey
Advancing Brain Research

THE UNIVERSITY OF MELBOURNE



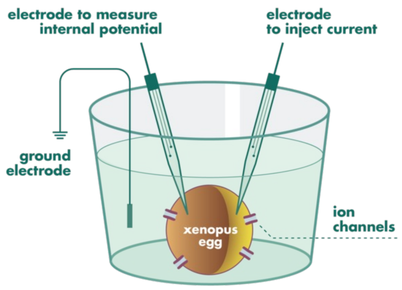
Professor Chris Reid

Email: christopher.reid@florey.edu.au

Project 1: Functional characterisation of HCN1 variants in developmental and epileptic encephalopathies

- **H**yperpolarization-activated **C**yclic **N**ucleotide–gated potassium channel isoform (**HCN**) channels play a key role in the pathogenesis of epilepsy.
- Twenty-eight pathogenic epilepsy variants in HCN1 have been identified.
- No clear predictive links between mechanistic dysfunction of the channel caused by the pathogenic variant and the clinical phenotype.
- This project aims to establish genotype-phenotype relationship by functionally characterising novel pathogenic HCN1 variants using a heterologous expression system (*Xenopus* oocytes).

Methods



- **Figure 1.** Configuration of two-electrode voltage-clamp electrophysiology using *Xenopus laevis* oocytes.

Correlating channel dysfunction with clinical phenotype

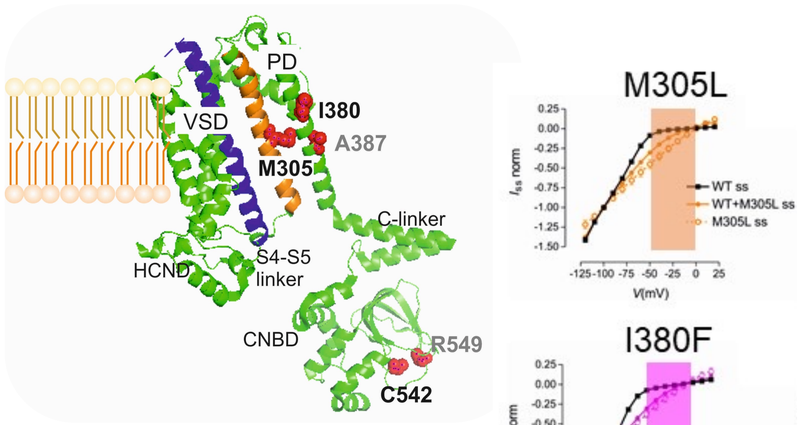


Figure 2. (Top) Structure of human HCN1 showing the locations of HCN1 mutations. (Right) Functional analysis revealed that the M305L and I380F variant results in significantly increased cation conductance.

Project 2: A mouse model of Tuberous Sclerosis Complex (TSC) and Focal Cortical Dysplasia Type II (FCDII) using *in utero* electroporation

- **T**uberous **S**clerosis **C**omplex (**TSC**) and **F**ocal **C**ortical **D**ysplasia type **II** (**FCDII**) are disorders caused by mutations of genes in the **m**ammalian **T**arget **O**f **R**apamycin (**mTOR**) pathway.
- These disorders are characterised by dysmorphic neurons in the cortex.
- Ectopic expression of **H**yperpolarization-activated **C**yclic **N**ucleotide–gated potassium channel isoform **4** (**HCN4**) in dysmorphic neurons contributes to seizures in a mouse model of TSC and FCDII.
- These neurons accumulate neurofilaments (NFs) in their soma and dendrites, as detected by SMI-311, a pan-neuronal NF antibody.
- Utilising *in utero* electroporation (IUE), we report the successful adoption of a mouse model of TSC/FCDII in our lab, which will be characterised.

Methods

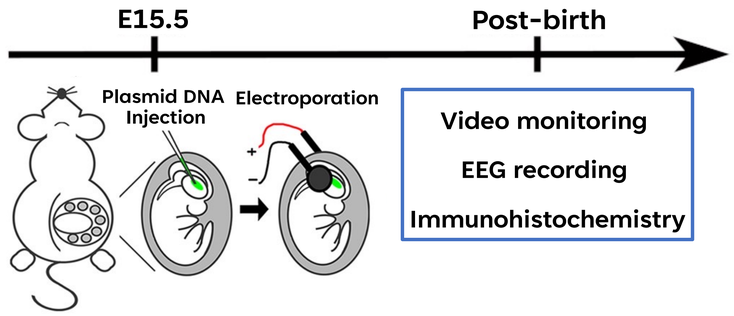


Figure 3. Outline of experimental methods, including the generation of mice by *in utero* electroporation and subsequent assessments performed. Adapted from Nguyen *et al*.

Mice injected with constitutively active Rheb have spontaneous seizures

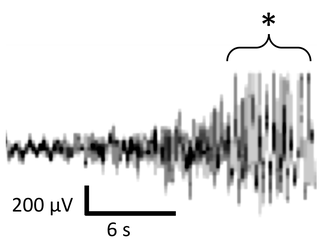


Figure 4. A representative EEG trace showing epileptiform seizure activity (asterisk).

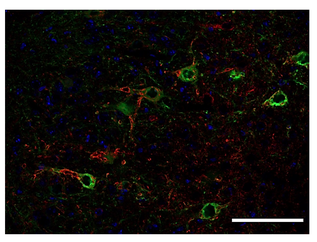


Figure 5. Confocal images for GFP (green) and SMI-311 (red) fluorescence in mouse cortical dysmorphic neurons co-stained with DAPI (blue). Scale bar = 100 µm

Mice injected with Rheb^{CA} displayed spontaneous seizures, detected in both video and EEG recordings. Rheb^{CA} mice show dysmorphic neurons as in human patients.

Project 3: Understanding cardiac factors underlying sudden unexpected death in epilepsy (SUDEP)

- SUDEP is the most common cause of premature death in epilepsy patients.
- Mechanism underlying SUDEP remains unclear but cardiac arrhythmia is suspected to play a role due to similarities with sudden cardiac death.
- Seizures are also known to alter cardiac function and importantly, variants in major cardiac arrhythmia genes (*KCNH2, SCN5A*) have been identified.
- Functional analysis in the lab revealed that *KCNH2* and *SCN5A* variants found in SUDEP cases result in dysfunctional channels.
- The aim of this study is to understand how dysfunctional cardiac channels lead to SUDEP using novel genetic SUDEP models, and if currently available treatment for cardiac arrhythmia can reduce SUDEP risk.

Methods

Figure 6. Mouse video EEG/ECG.

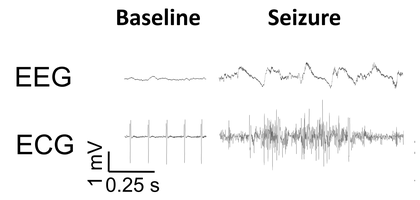


Figure 7. EEG/ECG recording in wild-type.

Dysfunctional *Kcnh2* increases risk of cardiac arrhythmia and premature death

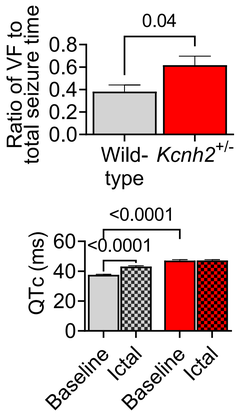


Figure 8. *Kcnh2*+/- mice experienced longer arrhythmia duration (top left) and corrected QT interval (bottom left).

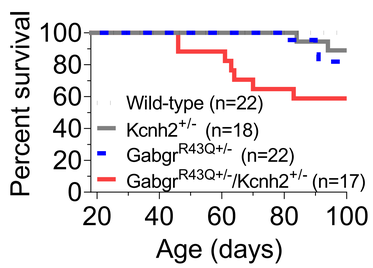


Figure 9. Combination of *Kcnh2*+/- and *Gabrg2*^{R43Q} reduced survival rate.

The Florey
Advancing Brain Research

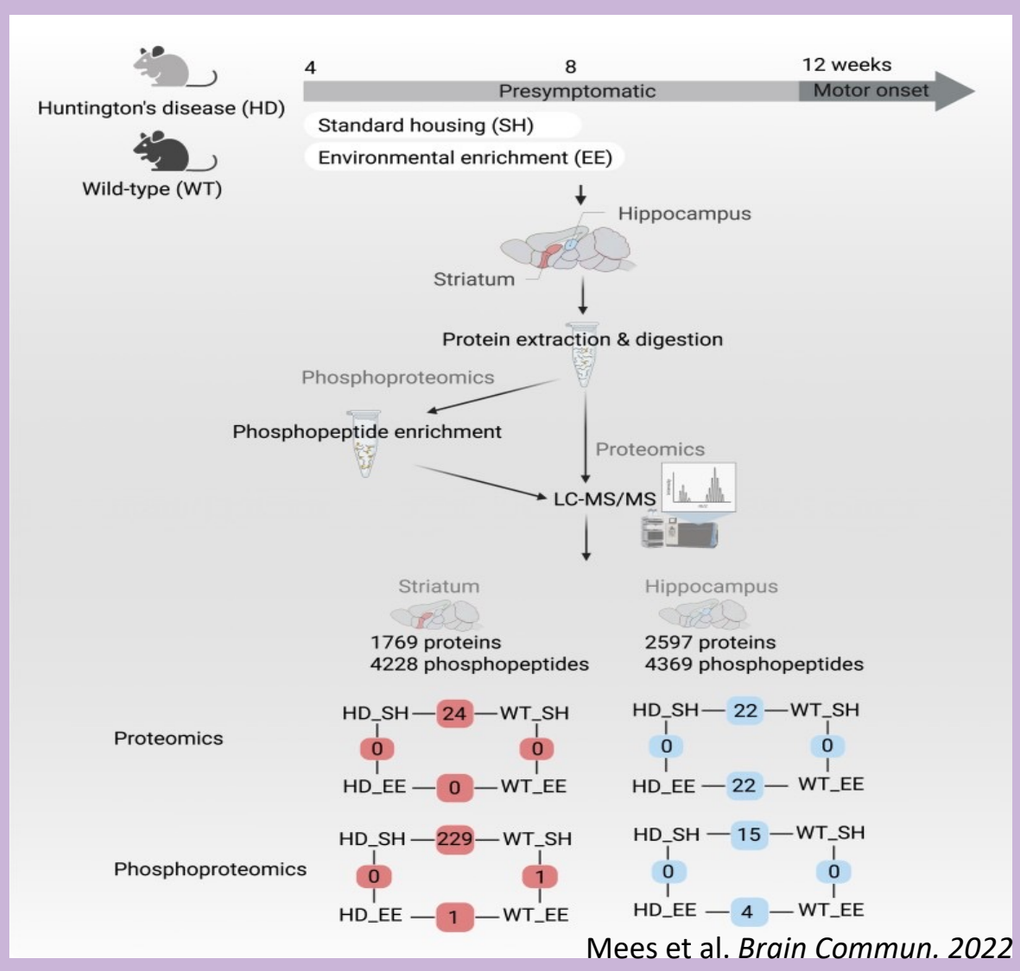
Genes Environment and Behaviour Lab

About our research

The Genes Environment and Behaviour group examines the mechanisms by which gene-environment interactions influence neurodegenerative (e.g. Huntington's disease and other dementias) and psychiatric disorders (e.g. depression, anxiety, schizophrenia and OCD).

We aim to understand how environmental and lifestyle factors such as stress, impact behaviour, cognition and physiology via dynamic molecular/cellular changes in the brain.

Along with exploring the mechanisms driving the beneficial effects of physical exercise, this research aims to identify new targets and study potential future therapies.



Mees et al. *Brain Commun. 2022*

Research interest key words

- Huntington's disease (HD)
- Obsessive-compulsive disorder (OCD)
- Depression/Anxiety disorders
- Environmental factors (e.g. Stress, physical activity/exercise)
- Neuropsychopharmacology (i.e. antidepressants, psychedelics, etc.)

Techniques

- Rodent behavioural studies
- Pharmacological and environmental interventions
- Immunochemistry
- Omics

Titles of projects available for 2024

- Therapeutic approaches to dementia and depression in Huntington's disease
- Studying gene-environment interactions in the pathogenesis of obsessive-compulsive disorder
- Therapeutic psychedelics in mental health
- Do the beneficial effects of exercise involve miRNA-mediated regulation of gene expression?

Contact information

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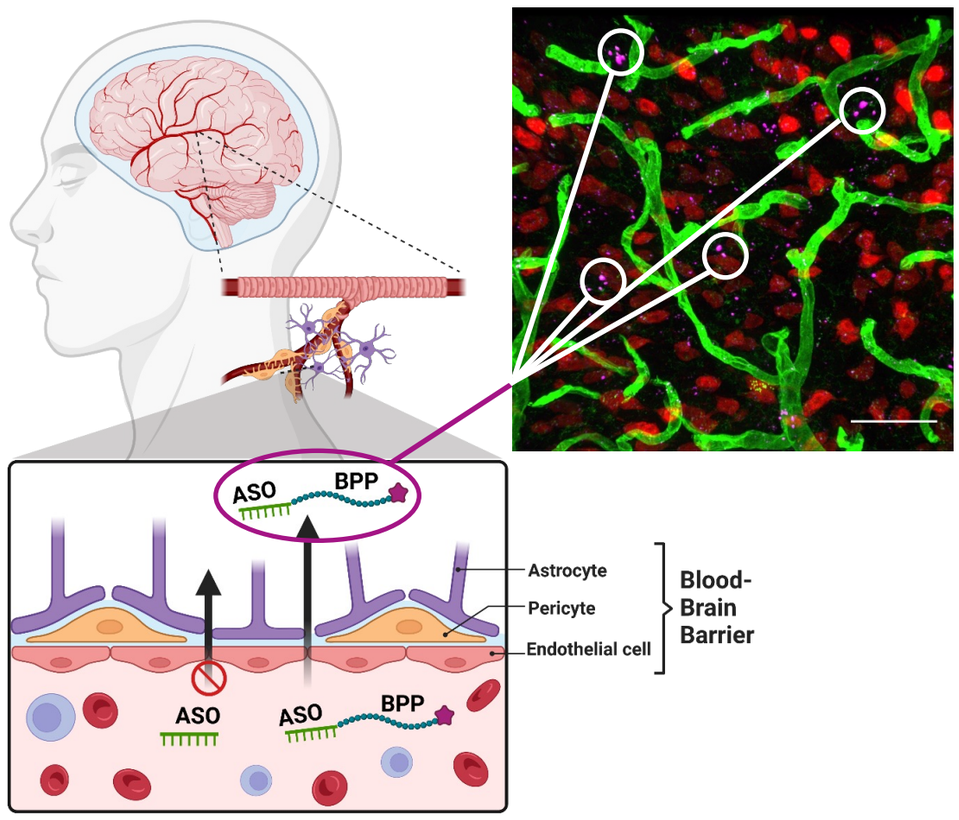
Florey Institute (Parkville Campus)

The Florey
Advancing Brain Research

Peptide and Oligonucleotide Therapeutics Group

About our research

Our research takes advantage of antisense technology to develop gene-specific antisense oligonucleotides (ASOs). ASOs are DNA-like molecules that can be used as genetic medicines for treating neurodegenerative diseases. Our group is also developing a peptide-based drug delivery system that can cross the blood-brain barrier, the barrier protecting the brain from harmful substances in the blood. By combining the molecular basis of this delivery system with therapeutic ASOs, we have created a unique and innovative therapeutic platform technology that is superior to other brain targeted ASO therapeutics.



Research interest key words

- Neurodegenerative diseases
- Antisense Oligonucleotides
- Therapeutic Peptides
- Blood-Brain Barrier-crossing Peptides
- CNS Drug Delivery System

Techniques

- ASO design and synthesis
- Peptide and Peptide-ASO Syntheses, HPLC analysis, purification and Mass spectrometry characterisation
- Cell-based assays, Molecular biology techniques (RNA extraction, cDNA synthesis, qPCR)
- Immunoassays (Western blot, Immunohistochemistry, Immunocytochemistry)
- Confocal and Fluorescent microscopy imaging (Live and fixed cells, and tissue section)

Titles of projects available for 2024

- Developing BBB-permeable ASO to target ataxin-2 and mitigate TDP-43 proteinopathies for amyotrophic lateral sclerosis therapy.
- Development of peptide-oligonucleotide conjugates to target poly (ADP-ribose) polymerase for new RNA-based amyotrophic lateral sclerosis therapy.
- Development of a novel CNS drug delivery platform based on lipopeptides.
- Developing the second-generation BBB-penetrating autophagy-inducing peptides as broad therapeutic modality for neurodegenerative diseases with proteinopathy.

Looking for

- Honours, Masters, and PhD students

Contact information

Dr Fazel Shabanpoor

Group Head

Fazel.Shabanpoor@florey.edu.au

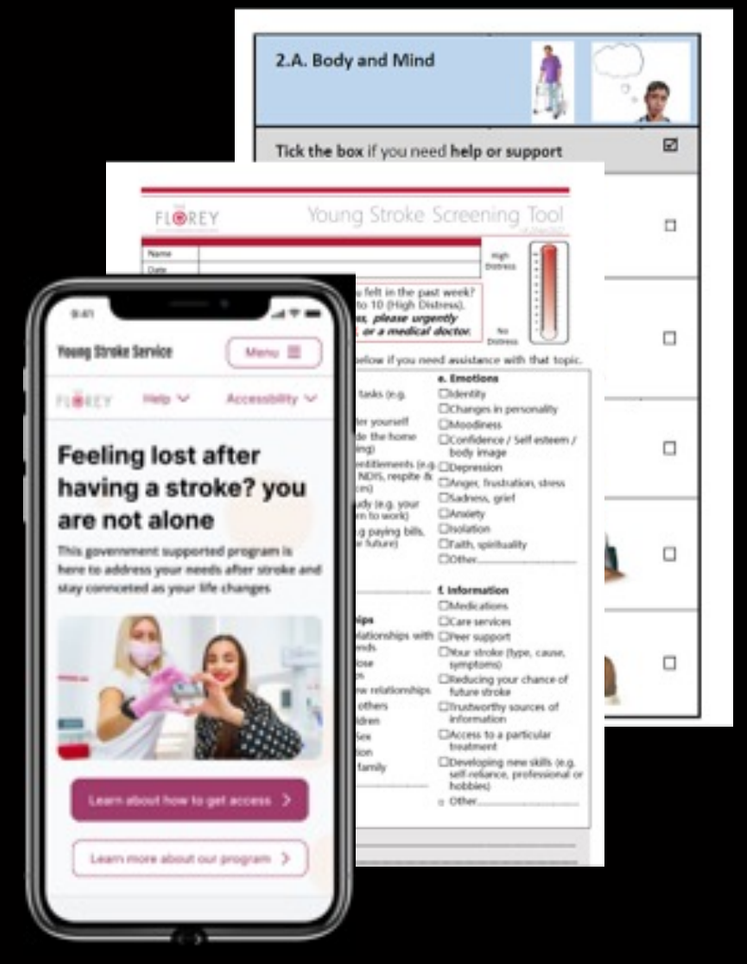
The Florey
Advancing Brain Research

Stroke Team, Austin Campus

About our research

Our group provides vital new research to improve stroke rehabilitation and recovery outcomes and practice worldwide. To impact the global burden of disability after stroke, we focus our efforts on:

- Building and testing treatments to reduce post-stroke disability in international trials (e.g., PESTO, AVERT DOSE).
- Acting as lead investigators in Australia's Centre of Research Excellence in Stroke Trials
- Developing new methods to innovate and redesign healthcare environments using Living Lab methods (NOVELL Redesign).
- Co-designing with young stroke survivors, and testing bespoke digital health services, and uniquely characterizing their recovery (Young Stroke Service for 18-45 year olds).
- Building global partnerships for transformational research (International Stroke Recovery and Rehabilitation Alliance (ISRRA)).



Research interest key words

- Stroke
- Young stroke
- Early rehabilitation
- Hospital (building) and service redesign

Techniques

- Clinical trials
- Deep phenotyping
- Co-design
- Living lab methods

Titles of projects available for 2024

- Leading development of the Young Stroke Service Deep Phenotyping project (Postdoctoral position 2025-2028)
- Implementation and evaluation of the Take Charge intervention for younger people affected by stroke

Looking for

- Honours students
- Master students
- PhD students
- Postdoctoral fellows

Contact information

Julie Bernhardt or Vincent Thijs
Group Heads
Via Nerida.larkin@florey.edu.au

The Florey
Advancing Brain Research

Motor Neurone Disease Group

About our research

Neurodegenerative diseases have a devastating impact on quality of life and impose a tremendous burden on the health care system. Motor neuron disease (MND) is the most rapidly fatal, with increasing physical disability and death typically within 2-3 years from symptom onset.

Our group has a broad interest in developing and delivering new therapeutics for MND using pioneering stem cell and animal models.

Research interest key words

- Motor neurone disease (MND)
- Amyotrophic lateral sclerosis (ALS)
- Primary lateral sclerosis (PLS)
- Spinal muscular atrophy (SMA)
- Kennedy's disease (KD)
- Frontotemporal dementia (FTD)

Techniques

- Immunohistochemistry
- Confocal microscopy and 3D image analysis techniques.
- Tissue cryostat sectioning
- Induced Pluripotent Stem Cells
- Organoids
- CRISPR

Titles of projects available for 2024

- Investigating age-related effects of autophagy on neuroglial cells
- Investigating autophagy pathway dynamics at the neuromuscular junction using mouse models
- Induced pluripotent stem cell-based organoid and cellular models for understanding disease mechanisms and identifying therapies for motor neuron disease
- Using DREADDs to deconstruct motor neuron disease
- Defining unique molecular markers of upper motor neurons in MND

Looking for

- Honours students
- Master students
- PhD students

Contact information

Professor Bradley Turner
Group Head
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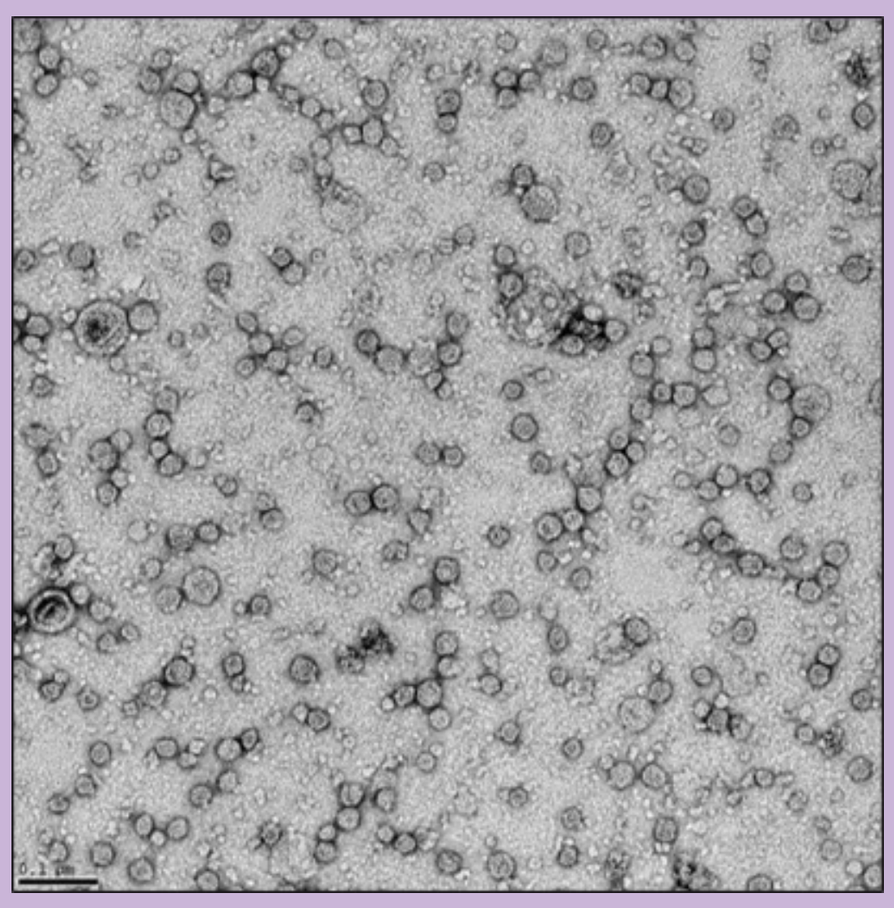
The Florey
Advancing Brain Research

Extracellular Vesicle Group

About our research

All cells in our body release tiny biological nanoparticles into their environment. These nanoparticles are called extracellular vesicle or ‘EVs’ for short. Extracellular vesicles are natures postal service, they deliver molecular information from cell to cell and around the body. Our team studies the contribution of EVs to the progression of dementia and brain cancer and uses EVs as a tool for identifying dysfunctional cellular pathways.

We aim to
1) gain insights about the biological origins of disease to identify novel therapeutic targets and
2) identify molecular species in EVs that could be used as disease biomarkers
3) use EVs to deliver neurotherapeutics



Research interest

- Extracellular vesicles (EVs)
- Alzheimer’s and Parkinson’s disease
- Brain cancer
- Extracellular vesicle biologics
- Extracellular vesicle based biomarkers

Techniques

- Isolation of EVs (size exclusion, density, tangential flow and ultracentrifugation)
- Characterisation of EVs (immunoblot, particle analysis, electron microscopy) and analytics (omics).
- Functional analysis (cell lines and in vivo)

Titles of projects available for 2024

- Autologous extracellular vesicle delivery of mRNA to the brain
- Understanding the journey of bacterial extracellular vesicles from the gut to the brain and the implications for neurodegenerative disease

Looking for

- Honours students
- Master students
- PhD students

Contact information

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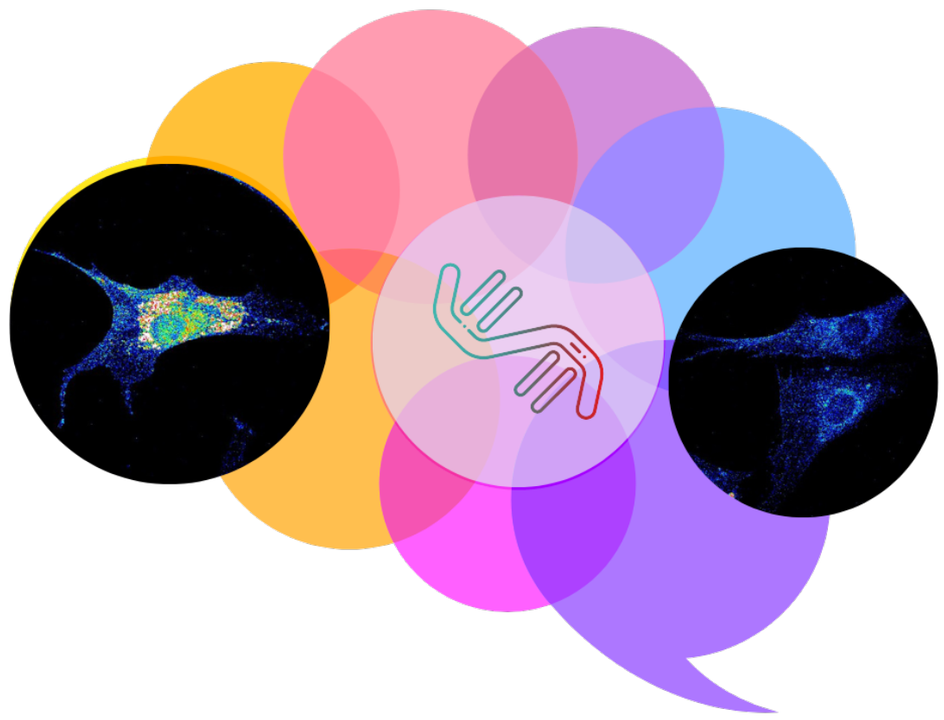
The Florey
Advancing Brain Research

mRNA Gene Therapy for the Treatment of Childhood Dementia

About our research

Without a cure or an effective treatment, childhood dementia robs a child's ability to learn, play, communicate, memories and eventually their lives before 18 years of age. Caused by over 100 genetic conditions, less than 5% of these genetic disorders have an approved treatment.



mRNA-based gene therapy can restore normal gene function. This project aims to develop clinically useful mRNA therapeutic formulations to treat genetic disorders causing childhood dementia, such as Niemann-Pick Disease Type C, Menkes disease, Wilson disease, Sanfilippo Syndrome, and Batten disease.

Project aims

- To develop an efficient brain delivery system for therapeutic mRNA
- To create a toolbox for designer therapeutic mRNA
- To assess mRNA therapeutic efficacy in disease models

Techniques

- Molecular biology/Biochemistry
- Cell biology
- Bioinformatics
- Animal handling

Research interest key words

- Childhood dementia
- mRNA gene therapy
- Genetic engineering
- Brain drug delivery

Looking for

- Honours students
- Master students
- PhD students

Contact information

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@HungYaHui

Championing Better Care for Young People with Stroke: Australia's New Young Stroke Service

K Borschmann[1], D Wong[2], E Power[3], T Rose[3], D Capurro[4], N Lannin[5,6], M Giummarra[5], D Cadilhac[1,5], B Parsons[1], L Murphy[7], K Hayward[1,4], T Withiel[8], A Brodtmann[5], C Bladin[9], M Crotty[10,11], V Thijs[1], J Bernhardt[1], on behalf of the Young Stroke Service project team.

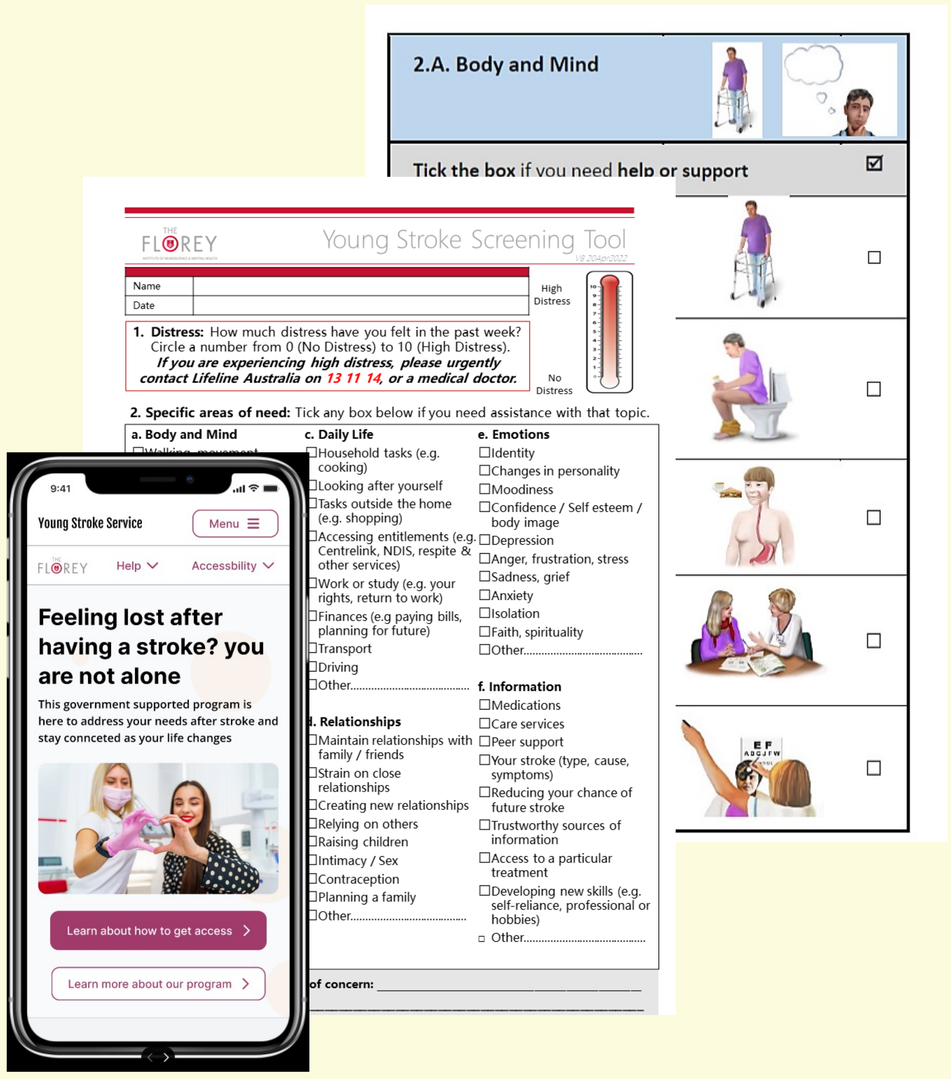
1. Florey Institute of Neuroscience and Mental Health, Melbourne, Australia. 2. La Trobe University, Melbourne, Australia. 3. University of Technology Sydney, Australia. 4. University of Melbourne, Australia. 5. Monash University, Australia. 6. Alfred Hospital, Melbourne, Australia. 7. Stroke Foundation, Melbourne, Australia. 8. Royal Melbourne Hospital, Melbourne, Australia. 9. Ambulance Victoria, Australia. 10. Flinders Medical Centre, Adelaide, Australia. 11. Flinders University, Adelaide, Australia.

BACKGROUND

- Too many young people with stroke report **unmet needs** related to their **age and life stage**.
- **Few health services** cater for young people with stroke.
- We aim to **improve access to appropriate services** for young people with stroke. We are building a dedicated, co-designed**, digitally supported** health service.

PROJECT AIMS

1. Establish a digital platform to engage with young adults with stroke.
2. Establish a suite of screening and assessment tools suitable for young people with stroke.
3. Validate new clinical pathways to access neurology and diagnostic support, neuropsychology, support for return to work and driving, assistance with NDIS applications.
4. Provide links to peer support and evidence-based stroke information, as well as specialised advice to clinicians.
5. Establish a patient dataset to inform future clinical research.



RESULTS

Patient enrolment

- The **first patient** was enrolled into the service in March 2023.
- **31** patients (average age 42) have registered into the service so far.
- **Referrals** were received from neurologists, rehabilitation physicians, allied health clinicians, nurses and GPs.
- Patients most commonly report that they have **needs** related to **fatigue, memory/ thinking**, and **return to work or study**.

Service delivery

- **Test sites** have opened at the **Austin Hospital** in Victoria, and **Flinders Medical Centre** in South Australia.
- **Specialised hubs** have opened for neuropsychological assessment and intervention, support for return to work, driving, and NDIS applications.
- Services are provided in-person and via telehealth.

Achievements

- **Lived Experience Contributors** provide input on most activities.
- Lived Experience Contributors receive **personalised support** when joining the project. This includes developing strategies to support **communication** preferences and strengths.
- **Ethical and clinical approvals** have been received for collation of core measures and clinical processes of all users for **evaluations**.
- **Health services** for young people with stroke have been mapped across Victoria and South Australia [poster #168 Giummarra et al].
- **Communication accessibility standards** have been developed.
- Principles established for **neuropsychological assessments** in young stroke, including a suite of measures and **patient feedback letters**.
- **Digital platform** is being developed, soon to launch.
- **Evaluations** of health economics, service provision, digital platform development, and user acceptability of the service are ongoing.

KEY MESSAGES AND STUDY OPPORTUNITIES

- The new Young Stroke Service **will fill important gaps** in diagnosis, treatment and ongoing support for young adults with stroke.
- Evaluations will inform clinical **policies and practice**, and sustainability beyond the grant period. We aim to expand nationally.
- Patients from Victoria and South Australia can now join the service.
- **Student projects** are available relating to diagnosis and post-stroke recovery in young people.
- **Contact us** for more information YoungStrokeAdmin@florey.edu.au.

YoungStrokeAdmin@florey.edu.au
www.youngstrokeservice.org.au

YSS collaboration powered by

PARTNERS

The Florey
Advancing Brain Research

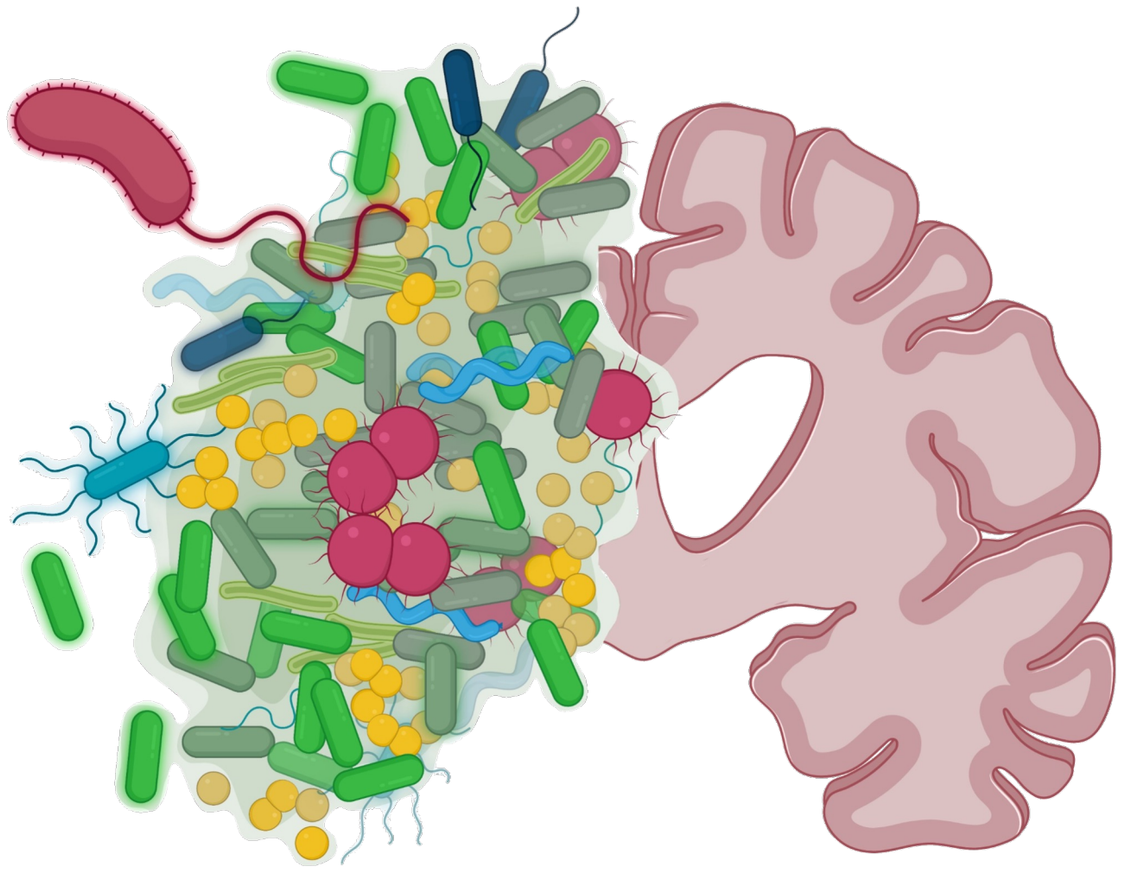
Neuroinflammation Laboratory

About our research

Taking the STING out of mind!

Our group seeks to elucidate the molecular events underlying disease-causing inflammatory responses in dementias and Motor Neuron Disease (MND) through the lens of neuro-immunology.

Our goal is to uncover specific immune-mediated neurodegenerative processes, enabling the development of tools for early disease diagnosis and treatment.



Research interest key words

- Neurodegenerative disease (MND and Tauopathy
- Neuroinflammation (Type I interferon)
- Sterile immunity (STING pathway)
- Aging

Techniques

- Molecular biology
- Advanced imaging
- Preclinical models
- Translational research

Titles of projects available for 2024

- Type I interferon Response Propagates TDP-43 Pathogenesis in ALS/MND
- Therapeutic Approaches for Tau-Associated Neuropathology
- Developing a Neuronal Model of DCTN1 Deficiency to Study Perry Syndrome

Looking for

- PhD students

Contact information

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