29TH NSW STEM CELL NETWORK HYBRID WORKSHOP

PARKINSON'S DISEASE AND REGENERATIVE MEDICINE

BRAIN AND MIND CENTRE, UNIVERSITY OF SYDNEY (VIRTUAL OPTION AVAILABLE)

Thursday, 12th May 2022
9am to 4pm

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The NSW Stem Cell Network gratefully acknowledge the support of Diabetes NSW & ACT and Brain and Mind Centre, University of Sydney.

WELCOME

This workshop has been put together to showcase the latest developments in regenerative medicine and Parkinson's disease. It will be run as a hybrid event to reach a greater audience, as we begin to emerge from COVID restrictions. Both options will offer an opportunity to engage with speakers and interact during our live Q&A sessions.

The day will start with session one, *Overview of Parkinson's Disease*. Professor Simon Lewis will provide a clinical overview and Professor Glenda Halliday will follow with a summary of Parkinson's disease pathology.

After morning tea, we will move onto the second session, which covers the rapidly expanding area of *Stem Cell Models*. Dr Nicolas Dzamko will explain how he is using stem cell-derived neural models to understand the cause of Parkinson's disease. Dr Niamh Moriarty will follow with a combined cell and gene therapy approach to treat Parkinson's disease. Kevin Law will outline novel approaches to improve safety and predictability of human stem cell grafts and lastly, Professor Joseph Powell will describe how he and his research group are using stem cell studies to identify the genetic causes of Parkinson's disease.

After lunch, we move on to *Therapeutics and Clinical Trials*, where we will hear from Professor Bernie Tuch about Living Cell Technology's NTCELL clinical trials using encapsulated porcine choroid plexus cells and Professor Peter Silburn will discuss deep brain stimulation as a current treatment option for Parkinson's disease. Professor Roger Barker will close out the session by providing a summary of where the field finds itself at the present time.

The last session of the day will be a panel discussion with all speakers, to discuss the future of Parkinson's disease.

This workshop would not have been possible without the support of The Brain and Mind Centre and our commercial sponsors, BlueChiip, Miltenyi, Stemcell Technologies and Evident. We encourage all attendees to visit their booths during the program breaks.

We hope you enjoy the workshop and continue to support the NSW Stem Cell Network at future events.

Keren Weiss
Manager
NSW Stem Cell Network

Prof Bernie Tuch
Director
NSW Stem Cell Network

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PROGRAM

9:00am	Registration opens/Light refreshments
9:30am	**Prof. Bernie Tuch - NSW Stem Cell Network** Welcome
Session 1	**Overview of Parkinson's Disease and Current Treatment Options** **Chair: A/Prof. Antony Cooper (Garvan Institute of Medical Research)**
9:40am	**Prof. Simon Lewis (University of Sydney)** Topic: Parkinson's disease: clinical overview and current management
10:05am	**Prof. Glenda Halliday (Brain and Mind Centre, The University of Sydney)** Topic: Pathology of Parkinson's disease
10:30am	Morning tea
Session 2	**Stem Cell Models** **Chair: A/Prof. Antony Cooper (Garvan Institute of Medical Research)**
11:00am	**Dr Nicolas Dzamko (The University of Sydney)** Topic: Stem cell-derived neural models for understanding causes and screening for potential treatments of Parkinson's disease
11:25am	**Dr Niamh Moriarty (The Florey Institute of Neuroscience and Mental Health)** Topic: A combined cell and gene therapy approach to treat Parkinson's disease
11:50am	**Kevin Law (The Florey Institute of Neuroscience and Mental Health)** Topic: Novel approaches to improve safety and predictability of human stem cell grafts for Parkinson's disease
12:15pm	**Prof. Joseph Powell (Garvan Institute of Medical Research)** Topic: Scaling stem cell studies to identify the genetic mechanisms of Parkinson's disease at cellular resolution
12:40pm	Lunch session
Session 3	**Therapeutics and Clinical Trials** **Chair: Prof. Simon Lewis (University of Sydney)**
1:40pm	**Prof. Bernie Tuch (Living Cell Technologies)** Topic: NTCELL: A disease modifying cell therapy for Parkinson's disease
2:05pm	**Prof. Peter Silburn (Queensland Brain Institute)** Topic: Deep brain stimulation as a treatment tool for Parkinson's disease
2:30pm	**Prof. Roger Barker (University of Cambridge)** Topic: Regenerative therapies for Parkinson's disease – where are we?
2:55pm	Afternoon tea
Session 4	**Panel Discussion** **Chair: Prof. Simon Lewis (University of Sydney)**
3:30pm	**All previous speakers** Topic: Future of Parkinson's Disease research
4:00pm	Refreshments/Networking

SPEAKER PROFILE

PROFESSOR SIMON LEWIS

Professor of Cognitive Neuroscience
ForeFront Parkinson's Disease Research Clinic
Brain and Mind Centre
School of Medical Sciences
University of Sydney

TALK TITLE

Parkinson's Disease: Clinical overview and current management

ABSTRACT

Parkinson's disease is the world's second most common neurodegenerative condition and from 1990 to 2015, the number of patients doubled to over 6 million and this number is projected to double again to over 12 million by 2040. The disease is progressive and characterised by a range of physical (motor) and non-physical (non-motor) symptoms, which result in high levels of burden and a reduced quality of life. Current therapies do nothing to slow this progression and symptomatic treatments typically offer partial and unsustained benefits with many patients entering residential care. This presentation will attempt to provide an oversight regarding the pharmacological and non-pharmacological approaches that are currently available, as well as highlighting the strategies underpinning ongoing and future disease modifying trials.

BIOGRAPHY

Simon Lewis is Professor of Cognitive Neuroscience at the University of Sydney and an NHMRC Leadership Fellow. He is the Clinical Director of the Ageing Brain Clinic and Director of the Parkinson's Disease Research Clinic at the Brain and Mind Centre and heads the NSW Movement Disorders Brain Donor program. He has published over 250 peer review papers, 2 books and 8 book chapters and has attracted over $5 Million in funding from various sources including the NHMRC, ARC and Michael J Fox Foundation to support his research interests targeting quality of life in neurodegenerative diseases.

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SPEAKER PROFILE

PROFESSOR GLENDA HALLIDAY

NHMRC Senior Leadership Fellow
The University of Sydney Faculty of Medicine and Health
Brain and Mind Centre
Sydney School of Medical Sciences

TALK TITLE

Pathology of Parkinson's Disease

ABSTRACT

Parkinson's disease has been recently redefined clinically and its underlying molecular biology determined. While it is a neurodegenerative disease, the loss of neurons is largely focal rather than large scale, and the symptoms are caused more by neurochemical deficits and dysfunctional cells than the loss of cells. The two main pathological features are the loss of dopamine neurons in the substantia nigra of the midbrain and the more widespread aggregation of a-synuclein in certain vulnerable neurons in the brain. Several triggers can cause the molecular cascade that kills dopamine neurons and makes the a-synuclein protein fibrilise and aggregate initially in brainstem neurons, including genetic variants and post-translational modification of the protein. The disease is slowly progressive (over decades) with the propagation of aggregates from vulnerable synapses to the entire neuron, and then from one neuron to other neurons and glial cells. Different mechanisms for propagation have been identified for these different brain cells which work in concert to sustain the slow disease process. Current therapeutic delivery of dopamine or deep brain stimulation temporarily relieve the symptoms with disease modifying treatments now able to be trialled due to identifying the underlying molecular biology.

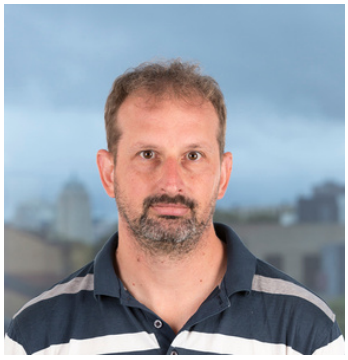
BIOGRAPHY

Glenda Halliday is an Australian career neuroscientist and research neuropathologist specialising in neurodegeneration. She has been a Research Fellow in the NHMRC and ARC systems since 1988. She was appointed Professor of Medicine (2003) then of Neuroscience (2008), then NHMRC Senior Principal Research Fellow (2010) at the University of New South Wales, and now NHMRC Senior Leadership Fellow located at the University of Sydney until 2025. She has worked with many Australian and international researchers on important scientific questions on Parkinson's disease, multiple system atrophy, dementia with Lewy bodies, frontotemporal dementias and motor neurodegenerative diseases. Her research has directly influenced clinical practice by providing the evidence base for understanding the pathologies underlying neurodegenerative diseases, clarifying the trajectory of these diseases over time and exploring any potential variability.

SPEAKER PROFILE

DR NICOLAS DZAMKO

Senior Research Fellow
School of Medical Sciences
University of Sydney



TALK TITLE

Stem cell-derived neural models for understanding causes and screening for potential treatments of Parkinson's disease

ABSTRACT

The development of induced pluripotent stem cell-derived neural models has greatly facilitated research into neurodegenerative Parkinson's disease. The ability to generate "brains in a dish" from patients with major Parkinson's disease risk mutations in genes such as leucine-rich repeat kinase 2 (LRRK2) and glucocerebrosidase (GBA) has provided new insight into the biological pathways dysfunctional in Parkinson's disease, and facilitated new models to develop and screen potential therapeutic compounds against genetic targets. Pathology found in Parkinson's disease brain tissue such as the upregulation of inflammatory pathways and alpha-synuclein protein can also be modelled, and again used to screen for potential therapeutic compounds. This presentation will highlight recent work from our team in these areas, and discuss future directions including the current development of bioprinted 3D midbrain models.

BIOGRAPHY

Nicolas Dzamko is senior research fellow at the University of Sydney working to advance understanding of neurodegenerative Parkinson's disease. His research team employs a combination of induced pluripotent stem cell models and primary cells/tissue to understand the biological pathways dysfunctional in Parkinson's disease, how they could be therapeutically targeted and if they can be developed into much needed biomarkers. He is a biochemist with a PhD from the University of Melbourne and undertook postdoctoral training at the MRC protein phosphorylation unit in Dundee Scotland and the University of NSW. He has been at the University of Sydney since 2018.

SPEAKER PROFILE

DR NIAMH MORIARTY

Postdoctoral Researcher
The Florey Institute of Neuroscience and Mental Health
University of Melbourne

TALK TITLE

A combined cell and gene therapy approach to treat Parkinson's disease

ABSTRACT

Clinical trials have demonstrated that the transplantation of new dopamine neurons into the brains patients with Parkinson's disease can provide long-term improvement in motor functions. The talk will provide a brief overview of the field of neural grafting and focus on our recent publication addressing the need and benefits of circuit reconstruction.

In the adult brain, the limited capacity for long-distance axonal growth means that cells are transplanted ectopically into the striatal target. As a consequence, several mDA pathways are not reinstated, which may underlie the incomplete restoration of motor function in patients. The viral delivery of GDNF to the striatum, in conjunction with homotopic transplantation of human pluripotent stem cell-derived mDA neurons, recapitulates brain-wide mDA target innervation. The grafts provided re-instatement of striatal dopamine levels and correction of motor function and also connectivity with additional mDA target nuclei not well innervated by ectopic grafts.

BIOGRAPHY

Niamh Moriarty is a postdoctoral researcher at The Florey Institute of Neuroscience and Mental Health, University of Melbourne. She completed a BSc (Hons) at the National University of Ireland. In 2018 she obtained her PhD in neurosciences before moving to Australia where she currently works under the mentorship of Professors Clare Parish and Lachlan Thompson. To date, her research career has focused on novel approaches to advance cell replacement therapy for Parkinson's disease She has 16 peer review publications, including first authorships in Cell Stem Cell and the Journal of Neuroscience and co-authorships in Nature Comms, Advanced Functional Materials and British Journal of Pharmacology. She has received a number of speaking invitations to national and international meetings and has been the recipient of many prizes and awards (including the John Collier postgraduate prize) and frequently reviews for a number of journals and philanthropic granting agencies.

SPEAKER PROFILE

MR KEVIN LAW

PhD Candidate
The Florey Institute of Neuroscience and Mental Health
University of Melbourne

TALK TITLE

Novel approaches to improve the safety and predictability of human stem cell grafts for Parkinson's disease

ABSTRACT

Clinical trials using human fetal tissue have demonstrated the transplantation of new dopamine neurons into the brains of Parkinson's disease patients to reverse motor symptoms. Human pluripotent stem cells now provide a more ethical, sustainable and standardised cell source – yet grafts remain heterogenous and have the risk of neural overgrowths. In recent years, our team has adopted 2 approaches to improve these challenges – (i) cell sorting to isolate enriched populations prior to transplantation and (ii) incorporation of a suicide gene into the donor cell to enable elimination of unwanted/proliferative cells from the graft after transplantation. In this talk, I will provide a brief summary on our cell sorting approach using reporter stem cell lines, yet focus on our recent and ongoing work using suicide gene (thymidine kinase) carrying stem cells and efforts to improve modulation of these 'kill switches' using bioengineered scaffolds for targeted drug delivery.

BIOGRAPHY

Kevin is a 4th year PhD candidate at The Florey Institute of Neuroscience and Mental Health, University of Melbourne. His research focus is on advancing stem cell therapy for brain repair, with a focus on Parkinson's disease and stroke. Kevin graduated from a Bachelor of Medical Science (Honours) at the University of Sydney. In 2017 he completed a 6-month internship at the University of Rochester (New York) investigating an astroglial cell therapy in Parkinson's disease, and under the supervision of Dr. Thomas Duncan and Prof. Michael Valenzuela, undertook an Honours research year in 2018, studying cognitive dysfunction in a canine model of Alzheimer's disease. During his PhD, he has co-authored publications in Nature Communications and the International Journal of Molecular Sciences and presented at conferences including the Australasian Neuroscience Society and Australasian Society for Stem Cell Research.

SPEAKER PROFILE

PROFESSOR JOSEPH POWELL

Garvan Institute of Medical Research
School of Medical Sciences, University of New South Wales

TALK TITLE

Scaling stem cell studies to identify the genetic mechanisms of Parkinson's disease at cellular resolution

ABSTRACT

Not available at the time of going to press.

BIOGRAPHY

Joseph Powell is the Director of Cellular Science at the Garvan Institute for Medical Research, and a Deputy Director of the UNSW Cellular Genomics Futures Institute. His research is focused on understanding the functional mechanisms by which genetic variants contribute to disease susceptibility at a cellular level, and ultimately achieve therapeutic and diagnostic outcomes. He has led capacity and community building in the space of cellular genomics technology nationally, establishing Platforms and Research Centres in Brisbane and Sydney, and co-founding the Oz Single Cell conference.

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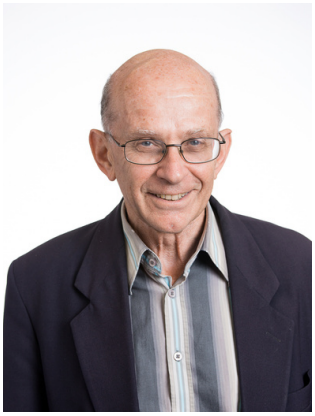
SPEAKER PROFILE

PROFESSOR BERNIE TUCH

IN CONJUNCTION WITH PROFESSOR CAROLYN SUE

Living Cell Technologies Ltd



TALK TITLE

NTCELL: A disease modifying cell therapy for Parkinson's disease

ABSTRACT

NTCELL are clusters of porcine choroid plexus that have been placed in microcapsules made from alginate. Choroid plexus produces cerebrospinal fluid and numerous growth factors, such as vascular endothelial growth factor, anti-oxidants and molecular chaperones. They are placed in the microcapsules to protect them from the immune system of the recipients in whom they are implanted for the management of Parkinson's Disease.

Studies in rats show that NTCELL survive for at least 18 months when implanted in the basal ganglia (J Neural Eng 2009; 6: 065001). In monkeys with MPTP induced PD, the cells survive for at least 6 months with improvement of neurological function and increase in expression of tyrosine hydroxylase both at the site of implantation and contralaterally (J Parkinson's Dis 2013; 3: 275). Two clinical trials conducted with NTCELL showed both safety and efficacy.In the 2012 phase 1b/2a study conducted in Auckland, one of the 4 recipients with late-stage PD showed a marked benefit for up to 4 years with a 23-point reduction from base line of the Unified PD Rating Scale (UPDRS) – motor function off medication.

The 2015 phase 2b study also showed efficacy with one group of recipients who had mid-to-late-stage PD showing a statistical difference from placebo for the UPDRS at 1 but not 2 years (Parkinsonism Related Dis 2021; 82: 128). Post hoc analysis showed a clinically significant effect (a decline in UPDRS of $\geqslant$ 6.45) out to 2 years for one of the treatment groups, and 18 months for another.

A third clinical trial is now being planned with larger numbers of recipients, and in the early to mid-stage of PD to determine the effect of NTCELL on altering the progression of the disease.

BIOGRAPHY

Bernie Tuch is the Executive Chairman of Living Cell Technologies Ltd (LCT) and is its interim CEO. He is a practising endocrinologist who has carried out a clinical trial with encapsulated insulin-producing cells for the treatment of type 1 diabetes. Indeed, it was because of this expertise that he was invited onto the Board of LCT in 2011. He still continues his research in diabetes, as part of the Australian Foundation for Diabetes Research, and is collaborating with the Israeli company Kadimastem Limited to try and bring stem-cell derived islet clusters in a bioengineered device to the clinic.

He completed his PhD at the University of Sydney in 1986, was a Professor of Medicine at The University of New South Wales 2000-9, at the University of Sydney 2014-21, and at Monash University since 2012. He was a Project Leader in the Division of Materials Science and Engineering at CSIRO.

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SPEAKER PROFILE

PROFESSOR PETER SILBURN

Asia-Pacific Centre for Neuromodulation
Queensland Brain Institute
University of Queensland

TALK TITLE

Deep brain stimulation as a treatment tool for Parkinson's disease

ABSTRACT

Not available at time of going to press.

BIOGRAPHY

Peter Silburn is a neurologist and world expert in the treatment and research of Parkinson's disease. He was honoured for his significant service to medicine as a neurologist, particularly in the treatment of neurodegenerative diseases' with appointment as a Member of the Order of Australia (AM) in the 2013 Australia Day Honours.

He is a founding member and lead clinician for the Asia-Pacific Centre for Neuromodulation, a joint initiative between The University of Queensland and St Andrew's War Memorial Hospital. He graduated from the University of Queensland in 1988. He commenced training in Neurology at Princess Alexandra Hospital, and completed training in Oxford at the Radcliffe Infirmary in 1995. He was subsequently the Clinical Lecturer in Neurology at the University of Oxford, United Kingdom. From Oxford, he went to the Karolinska Institute, Stockholm as a Research Fellow in the Department of Molecular Medicine. He then returned to Brisbane in July, 1996 where he commenced in private practice and began his university affiliations. He became a full Professor in Neurobiology at The University of Queensland in 2006. He maintains academic affiliations with Griffith University, Queensland University of Technology and the University of Queensland.

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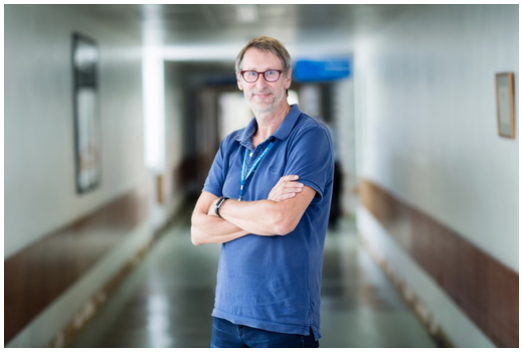
SPEAKER PROFILE

PROFESSOR ROGER BARKER

Professor of Clinical Neuroscience
Consultant Neurologist
University of Cambridge and Addenbrookes Hospital
Cambridge, United Kingdom



TALK TITLE

Regenerative therapies for Parkinson's disease - where are we?

ABSTRACT

One of the core pathological features of Parkinson's Disease is the loss of the dopaminergic nigrostriatal pathway which lies at the heart of many of the motor features of this condition as well as some of the cognitive problems. The importance of this pathological event is evident through the clinical benefits that are seen when patients with Parkinson's disease are treated with dopaminergic agents, at least in early stage disease. However, these agents create problems of their own. As such, there has been much interest in trying to better reconstitute the dopaminergic nigrostriatal pathway using factors to regrow it, cells to replace it or gene therapies to restore dopamine tone in the striatum. This talk will summarise where the field finds itself at the present time.

BIOGRAPHY

Roger Barker trained at Oxford University and then St Thomas Hospital in London. He has worked on regenerative therapies for Parkinson's disease since his PhD at Cambridge University in the early 1990s and has led several gene and cell based trial in this condition. His main research interests revolve around defining the clinical heterogeneity of Parkinson's disease and its basis with the aim of matching new therapies to specific disease subgroups. He also has done extensive research into Huntington's disease. He has published extensively, is a Director of the ISSCR and Director of the UK Regenerative Medicine Platform on Pluripotent Stem and Engineered Cells.

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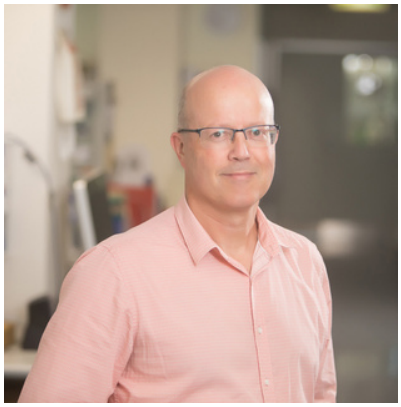
SPEAKER PROFILE

ASSOCIATE PROFESSOR ANTONY COOPER

Garvan Institute of Medical Research
Research Director, Australian Parkinson's Mission
University of New South Wales &
St Vincent's Clinical School (conjoint)



BIOGRAPHY

Associate Professor Antony Cooper is the Research Director of the Australian Parkinson's Mission (APM) and Head of the Neurodegeneration & Neurogenomics Laboratory at the Garvan Institute. He completed his Honours degree at the University of Otago prior to a PhD at McGill University in Montreal. Post-doctorate studies at the Institute of Molecular Biology (University of Oregon) preceded a tenured position as an Associate Professor at the University of Missouri. Recruited to the Garvan Institute of Medical Research in 2006, he has since focused his research on Parkinson's Disease with an emphasis on molecular mechanisms and genomics . He has been the recipient of research funding from the National Institutes of Health, NHMRC, Medical Research Future Fund, the Michael J Fox Foundation and Cure Parkinson's.

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The NSW Stem Cell Network is a professional community with an interest in all forms of stem cells. Our all inclusive free membership makes this network unique in consisting of not only researchers and practitioners, but members of the public, industry and government bodies. Our aim is to ensure effective communication between diverse sectors for the advancement of stem cell research. As a member, you will receive invitations to upcoming network and external stem cell-related events.

Sign up at www.stemcellnetwork.org.au

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CAREERS

To advertise positions related to the field of stem cells, please email a full description of the job offer to stemcellinfo@stemcellnetwork.org.au

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