25th NSW Stem Cell Network Workshop

Stem Cells and Neurological Injuries

Aerial UTS Function Centre
University of Technology Sydney, Ultimo, NSW
Monday 31st October 2016

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WELCOME

Welcome to the 25th Workshop of the NSW Stem Cell Network

'Neurological injuries' encompasses spinal cord injury (SCI), stroke, traumatic brain injury (TBI) and neural degenerative disease. There is no cure available for these traumatic injuries and the need for more effective therapies highlights the relevance of the 25th NSW Stem Cell Network Workshop.

We will start by exploring key molecular mechanisms of stem cells and our plenary lecturer will discuss a uniquely designed scaffold of human mesenchymal stromal stem cells (hMSC) with the potential to treat complications of SCI.

There are many exciting and promising findings coming from stem cell research in the laboratory now progressing to clinical trials. In session 2 experts in the field will be presenting results from current trials including an update on phase 1/2a trials in patients with subacute cervical spinal cord injury, NTCELL as a therapy for Parkinson's disease, NeuroRegan scaffold with stem cells for SCI repair and the clinical development of mesenchymal stem cells to treat chronic neurological injury.

We will also be discussing challenges in Australia with treatments for regenerative neurology.

Session 3 will explore how biology and engineering in this field have advanced with exciting new research on neural regeneration therapies.

By gathering key Australian and international experts, this event aims to provide opportunities for cross-disciplinary collaborations and enquiries, leading to more efficient translation of stem cell research. We hope that you take advantage of this unique occasion to discuss the main advances and issues in stem cell and regenerative neurology research with fellow leaders in the field.

The 25th NSW stem Cell Network Workshop would not have been possible without the generous help from our sponsors, speakers and all of you present today. We are truly grateful for your support and contribution.

We would also like to thank Professor Bryce Vissel, who was a major assistance in planning the Program.

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

Tamara Treleaven
NSW Stem Cell Network
Manager

Prof. Bernie Tuch
NSW Stem Cell Network
Director

PROGRAM

8:15am	Registration opens, light refreshment
8:50am	**Professor Bruce Milthorpe (University of Technology)** *Welcome*
Session 1	**Plenary Lecture** **Chair: Professor Bryce Vissel (University of Technology Sydney)**
9:00am	**A/Professor Yang (Ted) D. Teng (Harvard Medical School, USA)** *Synthetic matrix-assisted hMSC delivery: Defining recovery neurobiology of injured spinal cord*
10:00am	Morning tea
Session 2	**Clinical Trials** **Chair: Professor Bernie Tuch (NSW Stem Cell Network)**
10:20am	**Dr Edward Wirth (Asterias Biotherapies, USA)** *Update on a phase 1/2a trial of human embryonic stem cell-derived oligodendrocyte progenitor cells (AST-OPC1) in patients with subacute cervical spinal cord injury*
10:50am	**Dr Damien Bates (San-Bio, USA)** *Clinical development of MSCs for chronic neurological injury – the SanBio experience*
11:20am	**Dr Ken Taylor (Living Cell Technologies, New Zealand)** *NTCELL: A disease modifying cell therapy for Parkinson's disease*
11:40am	**Professor Simon Koblar (University of Adelaide)** *Australian challenges with regenerative neurology in stroke*
12:00pm	**Professor Jianwu Dai (Chinese Academy of Sciences, China)** *Clinical study of NeuroRegen scaffold with stem cells for spinal cord injury repair*
12:20pm	Lunch and Poster session
Session 3	**Biology and Engineering** **Chair: Professor Bryce Vissel (University of Technology Sydney)**
1:20pm	**Professor Henriette van Praag (NIH, USA)** *Regulation of structural and functional hippocampal plasticity by exercise*
2:00pm	**Professor Perry Barlett (The University of Queensland)** *Activating neurogenic precursors in the hippocampus can reverse cognitive impairment in aged animals*
2:40pm	**Dr James St John (Grittith University)** *Enhancing a glia-stem cell nerve bridge for spinal cord repair*

PROGRAM

3:00pm	**A/Professor David Nisbet (Australian National University)** *Promoting engraftment of transplanted neural stem cells in the brain using biofunctional scaffolds*
3:20pm	**A/Professor Mirella Dottori (The University of Melbourne)** *Human sensory neurons in a dish: A platform for developing treatments for peripheral neuropathies*
3:40pm	Afternoon Tea
Session 4	**Panel Session** **Chair: Chris Bertinshaw (Australasian Spinal Cord Injury Network)**
4:00pm	**Lead Discussants:** Professor Henriette van Praag A/Professor Yang (Ted) D. Teng Professor Perry Bartlett Dr Edward Wirth
5:00pm	Networking and close

Spinal Network

THOUGHT LEADERSHIP FORUM

The Spinal Network is holding a Thought Leadership Forum to discuss the value of quality and safety registries on Tuesday 15th November 2016.

The Forum starts at 12:00 noon with a light lunch and concludes at 5:00pm.
It will be held at the Stamford Grand Glenelg in Adelaide, South Australia.

SPEAKERS INCLUDE

- Emeritus Professor Phil Waite – Chair Spinal Network
- Associate Professor David Berlowitz – Institute for Breathing and Sleep
- Professor Kathy Rowan – Intensive Care National Audit & Research Centre (UK)
- Mr James Beresford – Director, Agile BI Pty Ltd
- Dr Philip Clayton – Editor, Australian and New Zealand Dialysis and Transplant Registry
- Dr Ralph Stanford – Spinal Surgeon, Prince of Wales Hospital

Attendance is free for member groups and their staff.

CLICK HERE TO REGISTER ONLINE NOW
Enquires phone 02 6263 5927
spinalnetwork.org.au

A/Professor Yang (Ted) D. Teng– Harvard Medical School, USA

A/Professor Yang (Ted) D. Teng received his Medical Degree and Master of Science in Neuropharmacology in Beijing University, Dr. Teng, then earned his Ph.D. degree in Cell Biology/Neuroscience at Georgetown University, Washington DC. For postdoctoral training, he focused on respiratory neurobiology, and stem cell biology and neurodegeneration at Georgetown University and Harvard Medical School, respectively. He is presently Professor and Director, Laboratory of Spinal Cord Injury, Stem Cell Biology & Neurofacilitation Research, Departments of PM&R and Neurosurgery, Harvard Medical School/Spaulding Rehabilitation Hospital/Brigham & Women's Hospital. He and his team investigate Functional Multipotency of Stem Cells and Recovery Neurobiology of the Spinal Cord through multimodal cross-examination approaches that integrate stem cell biology, neural and glial biology, chemical or genetic engineering, molecular pharmacology, and spinal cord oncology. Work of his team has received the prestigious 2011 Apple Award of the American Spinal Injury Association (ASIA), the ERF New Investigator Award from the Foundation of Physical Medicine & Rehabilitation (2004), and the Mayfield Awards and Larson Research Award from the Congress of Neurological Surgeons and American Association of Neurological surgeons (CNS/AANS) Joint Section on Disorders of the Spine and Peripheral Nerves (2012 and 2015). Dr. Teng reviews for ~50 academic and clinical journals, and holds study section membership for the NIH, DoD, EU academic organizations, and private foundations. He was elected President (2013-2014) of the American Society for Neural Therapy and Repair.

Synthetic matrix-assisted hMSC delivery: Defining recovery neurobiology of injured spinal cord

Mesenchymal stromal stem cells (MSCs) isolated from adult tissues offer tangible potential for regenerative medicine, given their feasibility for autologous transplantation. MSC research shows encouraging results in experimental stroke, amyotrophic lateral sclerosis, and neurotrauma models. However, further translational progress has been hampered by poor MSC graft survival, jeopardizing analysis of molecular and cellular bases for neural repair in vivo. We have now devised a human MSC (hMSC) delivery formula by investigating molecular events involving hMSCs incorporated in a uniquely designed poly(lactic-co-glycolic) acid scaffold, a clinically safe polymer, following inflammatory exposures in a dorsal root ganglion organotypic co-culture system. Also, in rat T9-10 hemisection spinal cord injury (SCI), we demonstrated that tailored scaffolding augmented hMSC stemness, engraftment, and function, resulting in robust motosensory improvement, neuropathic pain and tissue damage mitigation, and myelin preservation. Scaffolded hMSCs, not transdifferentiated, exerted multimodal effects of neurotrophism, angiogenesis, neurogenesis, anti-autoimmunity, and anti-inflammation. Hindlimb locomotion was restored by enhanced integrity of sub-midbrain circuits of serotonergic reticulospinal innervation, propriospinal projection network, neuromuscular junction, and central pattern generator. These regimens provided an adult stem cell platform for investigating molecular events underlying the repair impact of non-differentiated hMSCs. Our findings illuminate "recovery neurobiology" as a newly defined academic concept — the injured spinal cord (or brain), under proper conditions, may deploy polysynaptic neural circuits different from those of normal adulthood for post-injury functional improvement. The reestablished neural circuits and their molecular and cellular targets offer biological underpinning for development of clinical treatments including rehabilitation therapies to treat disabilities and complications of SCI.

Dr Edward Wirth - Asterias Biotherapies, USA

Dr Edward D. Wirth, III, M.D., Ph.D., is the Chief Medical Officer and joined Asterias in March 2013 after serving as Chief Science Officer at InVivo Therapeutics Corporation from 2011 to 2012. From 2004 to 2011, Dr. Wirth served as Medical Director for Regenerative Medicine at Geron Corporation, where he led the world's first clinical trial of a hES cell-derived product, GRNOPC1 in patients with subacute spinal cord injuries.

Dr. Wirth held academic appointments at Rush-Presbyterian St. Luke's Medical Center and at the University of Chicago from 2002 to 2004, and was a member of the faculty of the University of Florida from 1996 to 2002. Dr. Wirth received his Ph.D. and M.D. from the University of Florida in 1992 and 1994, respectively.

Update on a phase 1/2a trial of human embryonic stem cell-derived oligodendrocyte progenitor cells (AST-OPC1) in patients with subacute cervical spinal cord injury

The initial clinical safety of AST-OPC1 was evaluated in a phase 1 trial that enrolled five patients with neurologically complete T3-T11 thoracic spinal cord injuries (SCI). Based on the favorable safety data from that study, a phase 1/2a trial (SCiStar Study) was initiated to evaluate the safety and activity of AST-OPC1 in patients with motor complete ASIA Impairment Scale A or B (AIS-A or B) C5-C7 cervical SCI .

To date, there have been no intraoperative complications or serious adverse events (SAEs) related to AST-OPC1, the injection procedure, or immunosuppression with low-dose tacrolimus. Interim ISNCSCI exam data through Day 90 post-injection are currently available for all subjects in Cohort 1 and the first four subjects in Cohort 2.

The mean UEMS improvement at Day 90 relative to baseline was 5.0 points in Cohort 1 and 9.5 points in Cohort 2. All subjects have improved at least one motor level, and 2 of the 4 subjects in Cohort 2 have improved two motor levels on at least one side.

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Dr Damien Bates - San-Bio, USA

Dr Damien Bates is the Chief Medical Officer & Head of Research for SanBio, Inc. a stem cell company based in both Tokyo and Mountain View, California. Prior to his current position at SanBio, Dr. Bates has held senior executive & leadership roles in clinical development and medical affairs in multiple US based companies including Baxter, Organogenesis and Allergan. As Chief Medical Officer of Organogenesis, he successfully led the first and only BLA approval of an allogeneic cell based product in the US in 2012. Dr. Bates has also led the design and execution of over 20 IND, IDE and CTN studies across drugs, biologics and devices in the US and Asia and has had extensive regulatory interactions with the FDA, PMDA and EMA around the development and approval of cell based medicines.

Clinical development of MSCs for chronic neurological injury – the SanBio experience

Derived from mesenchymal stem cells obtained from healthy human adult donors, SB623 cells are generated under good manufacturing practices by transient transfection with a plasmid containing the human Notch-1 intracellular domain. These cells are implanted using stereotactic neurosurgical techniques to define target sites around injured brain tissue. Preclinical studies using models of chronic ischemic stroke and TBI have shown improvements in locomotor and global neurological function. Other preclinical studies have reported that SB623 cells are associated with the promotion of endogenous neural progenitor cell growth, differentiation and migration via various trophic factors. SanBio has recently completed a 2 year Phase 1/2a open label clinical study for patients with chronic motor deficits secondary to ischemic stroke. 12-month interim data from this study support the conclusion that SB623 cells are generally safe and well tolerated and demonstrate a significant improvement in the motor domain of neurological function after 12 months. Following this study, SanBio is now enrolling patients in two large double blind randomized controlled trials involving 156 patients with chronic motor deficits secondary to ischemic stroke in the US and 52 subjects with similar deficits secondary to TBI in the US and Japan.

Dr Ken Taylor - Living Cell Technologies Ltd, New Zealand

Dr Ken Taylor is the Chief Executive Officer of Living Cell Technologies Ltd. He graduated from the University of Otago,Dunedin ,New Zealand with BPharm.,MPharm (Hons) and PhD degrees in pharmaceutical chemistry and pharmacology. He completed a postdoctoral fellowship in Pharmacology and Experimental Therapeutics at the Johns Hopkins University School of Medicine in Baltimore, Maryland and subsequently held a joint appointment in neurosciences at Princeton University and the Squibb Institute of Medical research in Princeton, New Jersey.

In 1975 he joined Roche to establish a pharmacology research and clinical pharmacology program in Sydney, Australia and later was appointed Medical Director then Managing Director for Roche in New Zealand.

In 1990, after completing a business management program at IMD,Lausanne,Switzerland he was appointed Managing Director of Roche United Kindom based in Welwyn Garden City,Herts. Following the Roche aquistion of Syntex in 1994 he was appointed President, Syntex , Palo Alto, California to convert the corporate pharmaceutical company to Roche Bioscience, a research center. He later returned to New Zealand to manage the Roche affiliate and also to help Roche find research alliances in the Asia Pacific area.

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

NTCELL comprises encapsulated porcine neonatal choroid plexus cells that, when implanted into the putamen, act as a neurochemical factory secreting multiple neuroactive agents. Sustained clinical improvement has been observed in Parkinson's patients at 81 weeks post implantation.

Porcine choroid plexus cells produce a range of neurotrophic and growth factors (e.g. VEGF, IGFs and BDNF). The secretion of VEGF has been shown to provide a neuroprotective effect upon dopaminergic neurons in an experimental model of Parkinson's disease. Choroid plexus cells also release agents that are antioxidants and chaperone proteins responsible for removing plaque-generating proteins and neurofibrillary tangles. LCT has developed choroid plexus cells from a breed of domesticated pathogen free pigs. These cells are encapsulated in alginate microcapsules which permit the inward passage of nutrients and the outward passage of neural proteins and compounds normally secreted by choroid plexus cells, but

Professor Simon Koblar, University of Adelaide

Professor Simon Koblar is the inaugural Professor of Neurology and Neuroscience at the University of Adelaide. He is a clinician-scientist and his major areas of interest are regenerative neurology, molecular neurobiology, neural plasticity and the translation of basic and clinical scientific research in the field of stroke medicine. He has published over 100 peer-reviewed manuscripts and has had recurring NHMRC funding for over 20 years. He is founding Director of the Stroke Research Programme since 2005, which has a national and international reputation and is a unique collaboration of the South Australian Health and Medical Research Institute (SAHMRI), Basil Hetzel Institute, three Universities in SA, and the Central Adelaide Local Health Network. Prof Koblar has supervised 26 PhD, 3 Masters and 30 Honour students. He serves on the editorials boards for the International Journal of Stroke and Stem Cell Research and Therapy.

Australian challenges with regenerative neurology in stroke

Professor Koblar will present on his group's journey in using a *neural-type stem cell* from the tooth to enhance brain functional recovery following a stroke. The translation to a clinical trial is a challenge for all clinicians and scientists within Australia and he will speak of pathways to possibly overcome this into the future

Professor Jianwu Dai - Chinese Academy of Sciences, China

Dr. Dai has completed his PhD from Duke University and postdoctoral studies from Harvard Medical School. He is now the Director of the Center for Regenerative Medicine, Institute of Genetics and Developmental Biology at Chinese Academy of Sciences.

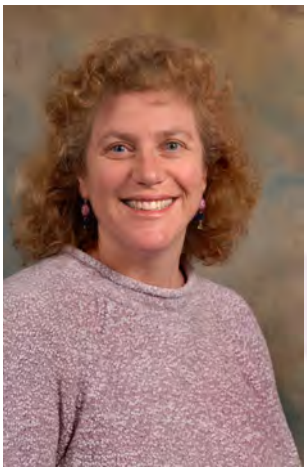
Dr Dai has developed functional growth factors and stem cell binding collagen scaffolds which could actively induce a variety of tissue regeneration. He has published over 140 papers in reputed journals in the field of regenerative medicine and has been serving as an editorial board member of Biomaterials. Dr Dai has led several tissue regenerative clinical studies including spinal cord injury repair.

Collagen scaffolds with stem cells for spinal cord injury repair: From animal models to clinical study

Spinal cord injury (SCI) is a devastating injury resulting in changes in the spinal cord's motor, sensory, or autonomic functions.

Following SCI, an inhibitory environment develops at the injury site to inhibit neural regeneration. We have developed a functional biomaterial consisting of collagen scaffolds (NeuroRegen scaffolds) and biologically active molecules (neurotrophic factor or the antagonists to myelin-associated inhibitor), and stem cells to build a nerve regeneration microenvironment. Specifically, (1) the linear ordered collagen based NeuroRegen scaffold was developed to guide the neural regeneration along its fibers and decrease the formation of glial scars, (2) collagen binding neurotrophic factors were incorporated into the scaffolds to promote neuronal survival and neural fiber regeneration, (3) antagonists to myelin-associated inhibitors were added to the scaffold to direct the neuronal differentiation of neural stem cells at the injury site, (4) Mesenchymal stem cells (MSCs) were also added to the scaffold to reduce the acute inflammatory response due to SCI. These strategies were found to promote neural regeneration and functional recovery in SCI animals. NeuroRegen scaffolds with stem cells are in the clinical study of spinal cord injury repair.

Professor Henriette van Praag - NIH, USA



Professor Henriette Van Praag received her Ph.D. from Tel-Aviv University, Israel in 1992 for her work studying the development of opiate receptor function with Dr. Hanan Frenk. She did her postdoctoral research on the role of nerve growth factors in brain injury at Robert Wood Johnson Medical School in New Jersey with Dr. Ira Black from 1992-1997.

She continued her research in brain regeneration as a staff scientist with Dr. Fred Gage in the Laboratory of Genetics at the Salk Institute for Biological Studies in La Jolla, California from 1997-2007. Specifically, she researched the regulation of the birth of new neurons in the adult hippocampus, a brain area that is important in learning and memory, and made significant discoveries pertaining to the regulation of neurogenesis, synaptic plasticity and memory function by exercise. She also utilized retroviral vectors to provide the first evidence for the functional integration of new neurons into the adult hippocampus.

Regulation of structural and functional hippocampal plasticity by exercise

Most neurons in the adult central nervous system are terminally differentiated and cannot be replaced when they die. However, research over the past two decades has shown that small populations of new neurons are generated in the mature olfactory bulb and the hippocampus. In the adult hippocampus, newly born neurons originate from putative stem cells that exist in the subgranular zone of the dentate gyrus. Interestingly, the production, survival and functional integration of newborn hippocampal cells can be regulated by a variety of environmental and neurochemical stimuli. In particular, voluntary exercise in a running wheel is correlated with increased neurogenesis and enhanced synaptic plasticity in the dentate gyrus. Enhanced neurogenesis is associated with improved spatial navigation and pattern separation in adult rodents, indicating that newborn hippocampal cells play a role in cognition. Ongoing studies pertain to understanding the effects of exercise on network organization and synaptic plasticity of newly born neurons in the adult brain. In addition, peripheral factors that may elicit the beneficial effects of exercise on brain and behavior are researched. The identification and potential mechanism of action of a novel myokine that plays an important role in adult hippocampal neurogenesis and cognition will be discussed.

Professor Perry Bartlett - The University of Queensland

Professor Perry Bartlett is Professor Perry Bartlett has been responsible for a series of ground-breaking discoveries in neuroscience, which have often overturned existing dogma and led to a new understanding, particularly in the areas of neuronal precursor regulation and neuron survival in the developing and adult nervous system. Most prominent amongst these, was his laboratory's discovery in 1992 of the presence of stem cells in the adult brain that had the capacity to produce new neurons. His group was first to isolate and characterise these stem cells in 2001, and more recently revealed the presence of a latent hippocampal stem cell population that influences learning and memory.

He was the inaugural Director of the Queensland Brain Institute (2003-15), at The University of Queensland, and holds the Foundation Chair in Molecular Neuroscience. Previously he was Head of the Division of Development and Neurobiology at the Walter and Eliza Hall Institute of Medical Research. He is a Fellow of the Australian Academy of Science (FAA), a past NHMRC Senior Principal Research Fellow and ARC Federation Fellow, and a past President of the Australian Neuroscience Society. He has championed interactions with China establishing three joint neuroscience laboratories in China, two with the Chinese Academy of Sciences and one with the Second Military Medical University, where he also holds an Honorary Professorship. He has published >245 papers, many of which have appeared in the most influential journals and have attracted over 16,300 citations. He has an h-index of 68.

Activating neurogenic precursors in the hippocampus can reverse cognitive impairment in aged animals

The production of new neurons in the hippocampus of adult mice, shown to be important for regulating some forms of learning and memory, decreases substantially as the animals age, with little or none in animals > 18 months. Coincident with this decrease is the significant impairment to spatial learning suffered by the aged animals, suggesting the two may be linked.

In 2008, we discovered the presence of a quiescent population of neurogenic precursors even in the very old animals and begun investigating their molecular regulation in order to determine its effects on learning and memory. Exercise is known to increase hippocampal neurogenesis in younger animals, and our recent studies have revealed that aged animals require a different, but precise length of exercise for activation to occur. Only animals which run for this precise period show a significant recovery in spatial learning, almost to the level of young controls. Moreover, we show that ablating the production of the new neurons following precursor activation completely ablates this recovery, indicating the effect is mediated by this mechanism. We have defined some of the molecular regulators mediating this improvement, and believe they may have future application in ageing humans with cognitive decline.

Dr James St John - Griffith University

Dr James St John is Head of the Clem Jones Centre for Neurobiology and Stem Cell Research at Griffith University, Queensland. He obtained his PhD in Agricultural Science from the University of Melbourne in 1996. He then applied his expertise in carbohydrate synthesis and manipulation to determining the role of carbohydrates in the development and regeneration of the mammalian brain. He held positions as a Peter Doherty NHMRC post-doctoral fellow at the University of Melbourne and University of Queensland.

In 2007 he took up the position of Group Leader of the Olfactory and Spinal Cord Repair Laboratory at the Eskitis Institute for Drug Discovery at Griffith University. In May 2016 he became Head of the Clem Jones Centre for Neurobiology and Stem Cell Research, with the aim of the Centre being to develop therapies to treat acquired brain injury and spinal cord injury. Recent funding from the Perry Cross Spinal Research Foundation has enabled the targeted development of a cell transplantation therapy for spinal cord repair.

Enhancing a glia-stem cell nerve bridge for spinal cord repair

Can spinal cord paralysis be treated by transplantation of cells from the nose? A recent exciting proof-of-principle trial in humans has shown that functional regeneration can be achieved after transplanting olfactory glia in the injured spinal cord. These glia are specialised cells that have a remarkable ability to aid nerve cells to grow. What is now needed is to improve the transplantation therapy to make it more effective and to combine neural stem cells together with the glia.

The team led by Dr James St John is targeting numerous aspects of the therapy including the surgical transplantation procedure, the production of three-dimensional nerve bridges, and the delivery of physiotherapy. For the development of the three-dimensional nerve bridges we have developed a new 3D culturing protocol that results in dramatically improved cell growth and behaviour. When cultured in floating liquid marbles, cell proliferation and migration are significantly increased and, perhaps most importantly, cell-cell interactions occur that replicate in vivo cell interactions. We have also identified that the phagocytic activity of olfactory glia, but not Schwann cells, can be stimulated up to 20 fold by the natural product curcumin indicating that the two closely related glial cell types have distinct characteristics relevant for neural regeneration therapies.

In addition, the natural product RAD288 can stimulate the proliferation of Schwann cells, while the structurally related product RAD289 stimulates the migration of Schwann cells. These results demonstrate that specific activities of glial cells can be targeted to potentially fine tune their therapeutic use for neural repair therapies. Overall, the combination of cell biology, chemistry and engineering is leading to improved 3D cell preparations for neural repair therapies.

A/Professor David Nisbet - Australian National University

Dr Nisbet's research deals with the fabrication of synthetic cellular microenvironments that support stem cell survival, adhesion and promote differentiation. Currently he has been investigating the feasibility of using biodegradable electrospun nanofibres and injectable hydrogels (synthetic and natural) to control stem cell behaviour both in vitro an in vivo. His approach is to attempt to fabricate a synthetic niche microenvironment for stem cells, whilst optimizing the interfacial features to providing biochemical and biological support (i.e. a combination strategy utilizing tethered growth factors; or viral vectors and/ or stem cells). Now at 7 years post-PhD, I have had the benefit of research experience at 2 of the top Universities in my field (Toronto and UC Berkeley) and have established an independent research group at ANU that bridges the Research School of Engineering and the John Curtin School of Medical Research.

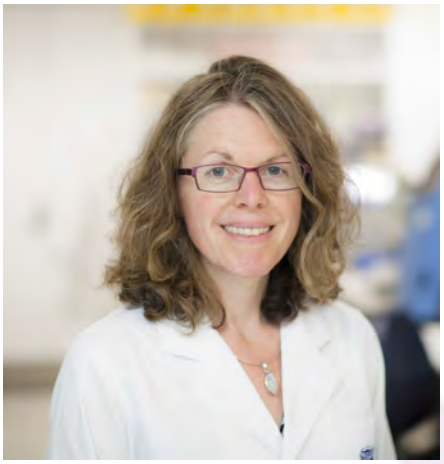
Promoting engraftment of transplanted neural stem cells in the brain using biofunctionalised scaffolds

Extracellular matrix (ECM) mimicry is important in tissue engineering in order to provide physical and chemical cues that will promote cell survival. Biomaterials such as nanofibrous scaffolds and hydrogels have played an important role in providing physical support to cells both *in vitro* and *in vivo*. Providing chemical support is equally important as the presentation of proteins at varying concentrations could allow us to direct cell behavior, including migration and differentiation.

Previously, we tethered brain derived neurotrophic factor (BDNF) to poly-caprolactone nanofibrous scaffolds using a chemical crosslinker[1]. We found that these functionalized scaffolds promoted neural stem cell proliferation and directed cell differentiation. In addition, we showed that immobilizing BDNF to the scaffold improved cell survival compared to cells cultured on scaffolds with soluble BDNF. More recently, we used this same immobilization method for attachment of glial cell derived neurotrophic factor (GNDF) and assessed its biofunctionality in the brain parenchyma[2]. With such convincing results, this crosslinking technique can now be transferred to short electrospun polymer nanofibers as an immobilized growth factor delivery mechanism.

Here we developed a composite scaffold, incorporating short nanofibers embedded within a thermo-responsive hydrogel, as a means to transplant neural progenitor cells into the injured brain. We functionalized this composite scaffold with glial derived neurotrophic factor (GDNF), a protein known to promote cell survival and axonal growth. This was either blended into and/or covalently attached onto the elements within the composite scaffolds to control the delivery. In Parkinsonian mice, we show that these composite scaffolds enhanced the survival of neural progenitor cell grafts and reinnervation of the striatum, whilst also having minimal impact on the host immune response. Our composite scaffold enhanced the survival and integration of grafted neurons within the injured brain. ***David R. Nisbet***[1] *Clare Parish*[2 1] Research School of Engineering, College of Engineering and Computer Science, The Australian National University. [2] Florey Institute of Neuroscience & Mental Health, The University of Melbourne, Parkville, VIC 3010, Australia[1]M. K. Horne, D. R. Nisbet, J. S. Forsythe, C. L. Parish, *Stem Cells and Development*. **2009**, *19*, 843-52. [2]T. Y. Wang, J. S. Forsythe, C. L. Parish, D. R. Nisbet, *Biomaterials*. **2012**.

A/Professor Mirella Dottori - The University of Melbourne



A/Professor Mirella Dottori is an ARC Future Fellow and Group Leader of the Stem Cell Laboratory at the Centre for Neural Engineering, University of Melbourne, Australia. A/Prof Dottori undertook her PhD at Walter and Eliza Hall Institute in the field of developmental neuroscience. Her studies in this area continued into her postdoctoral training at the Salk Institute, La Jolla, USA. She then returned to Australia as a NHMRC Howard Florey Fellow working at Monash University to study human stem cell biology. In 2007, A/Prof Dottori established her own research group at the University of Melbourne. The major focus of her studies is to utilize human pluripotent stem cells to create cellular models of brain development and neurodegenerative diseases.

Human sensory neurons in a dish: A platform for developing treatments for peripheral neuropathies

The fundamental purpose of the sensory nervous system is to receive and transmit information to the brain, which initiates how we interpret our external world and consequently influences what responses will be made. The dorsal root ganglia (DRG) form part of the sensory nervous system, which enables us to sense temperature, pressure, position and pain. It is evident that peripheral sensory neurons, particularly DRG neurons, can regenerate more easily than the neurons of the central nervous system. Despite this regenerative potential, there are vast ranges of diseases and conditions, usually progressive, which cause sensory peripheral neuropathies. These can be severely debilitating and in many cases, there is no treatment available for the disease. It would be invaluable to have an *in vitro* system of functional human sensory neurons to study their development, regenerative potential and help fast-track therapies to treat severe sensory neuropathies. We have developed a robust protocol for deriving DRG sensory neurons from human pluripotent stem cells (hPSCs) and shown that they consist of heterogeneous neuronal subtypes expressing similar markers as described in the adult rodent DRG. Using microelectrode arrays and immunostaining analyses, we observe that hPSC-derived DRG neurons display phenotypic specification and functionally mature within 8 weeks in culture. These studies are highly significant for understanding the development, molecular and functional characteristics of human DRG sensory neurons, which can then be applied for developing therapies to treat peripheral sensory neuropathies.

Posters

1. Adult skin-derived neural precursors—A candidate for autologous neuroreplacement therapies

Duncan T[1], Lowe A[1], Siette J[1], Sidhu K[2], Westbrook F[3], Sachdev P[4], Chieng B[5], Lewis T[6], Lin R[7], Sytnyk V[8], Valenzuela M[1]. Regenerative Neuroscience Group, Brain and Mind Centre, University of Sydney, Sydney, NSW 2050. Stem Cell Laboratory, University of New South Wales, Sydney, NSW 2031. School of Psychology, University of New South Wales, Sydney, NSW 2052. Centre for Healthy Brain Ageing, University of New South Wales, Sydney, NSW 2031. Behavioral Neuroscience Laboratory, Brain and Mind Centre, University of Sydney, Sydney, NSW 2050. School of Medical Sciences, University of New South Wales, Sydney, NSW 2052. Asbestos Diseases Research Institute, Bernie Banton Centre, Concord Hospital, Sydney, NSW 2139. School of Biotechnology and Biomolecular Science, University of New South Wales, Sydney, NSW 2052

2. Spontaneous neuronal repopulation within the dorsal hippocampus following an acute kainic acid-mediated excitotoxic injury

Authors: **Yu Shen Yin[1,2]**, Lyndsey Konen[2], Christopher W. Vaughan[1], Bryce Vissel[2,3,4] [1]Kolling Institute of Medical Research, University of Sydney [2]Garvan Institute of Medical Research [3]Faculty of Science, University of Technology Sydney [4]Faculty of Medicine, UNSW Australia

3. Multiple sclerosis, a disease in a dish

Naomi Koh Belic, Matthew Padula, Innocent Macha, Bruce Milthorpe, Jerran Santos.

Advanced Tissue Regeneration and Drug Delivery Group, University of Technology Sydney, Ultimo, NSW 2007, Australia

4. The kynurenine pathway of tryptophan metabolism modulates neural stem cell proliferation

Juliana Croitoru-Lamoury[1,6], Francois M. J. Lamoury[1,6], Edward Walters[2], Kazuo Suzuki[1], David Walker[3], Simon P. Jones[1], **Michael D Lovelace[1]**, Rosanne Taylor[5] and Bruce J. Brew[1,6] [1]St Vincent's Centre for Applied Medical Research and [6]Department of Neurology, St. Vincent's Hospital, Sydney NSW, Australia [2] University of Notre Dame Australia, Sydney NSW, Australia [3] Department of Physiology, Monash University, Clayton VIC, Australia [5] Faculty of Veterinary Science, University of Sydney, NSW, Sydney, Australia [6] These authors contributed equally to this work

Notes

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