NSW StemCell NETWORK

28th NSW Stem Cell Network Workshop

Stem Cell Innovative Technologies

The Illawarra Health and Medical Research Institute
University of Wollongong, NSW
Tuesday 11th June 2019

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WELCOME

Welcome to the 28th Workshop of the NSW Stem Cell Network

This regional Workshop has been put together to in-service researchers and others in the Wollongong area on the latest developments in stem cells and regenerative medicine.

The Workshop would not have been possible without the financial support of the Illawarra Health and Medical Research Institute (IHMRI) as well as the University of Wollongong. Our commercial sponsors STEMCELL Technologies, Lonza, Miltenyi Biotec, TRICEP and the ARC Centre of Excellence for Electromaterials Science (ACES) have also been of help . We encourage all attendees to visit their booths during the program breaks.

The local organsing committee of Associate Professors Mirella Dottori, Jeremy Crook and Dr Lezanne Ooi; Thanks go to them who selected the exciting speakers who will be challenging you today.

We start the day with session one Disease Modelling. Key note speaker Dr Michael O'Connor will tell us about his original research using pluripotent stem cells to make lenses as a treatment for cataracts. In the second session after morning tea, we cover the rapidly expanding area of Bio-engineering. This starts with the keynote speaker Dr Anita Quigley speaking on development of 3D scaffolds for tissue regeneration and interfacing with bionic devices. After lunch, we move to Therapeutics starting with Dr Serena Duchi telling us about bone and cartilage repair to treat osteosarcoma and rebuild compromised cartilage to prevent osteoarthritis.

To finish the day, we have a panel of experts who will be challenged with topical issues including the use of autologous cells. We hope that the panel will be able to provide practical advice about how to tap into the stem cell funds recently announced by the federal government.

Enjoy the day and most importantly be involved and ask the presenters including those with posters questions.

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

Tamara Treleaven	Prof. Bernie Tuch
NSW Stem Cell Network	NSW Stem Cell Network
Manager	Director

PROGRAM

9:30 am	**Registration opens**
10:00 am	**Professor David Adams (Illawarra Health and Medical Research Institute)** *Opening address*
Session 1	**Disease Modelling**
10:05 am	**Dr Michael O'Connor (University of Western Sydney)** *Pursuing improved cataract treatments through pluripotent stem cell research*
10:45 am	**Dzung Do-Ha (University of Wollongong)** *Investigating changes in neuronal excitability using iPSC-derived motor neurons from ALS patients*
11:00 am	**Dr Dhanisha Jhaveri (Mater Foundation, Queensland Brain Institute, University of Queensland)** *Targeting adult-born hippocampal neurons for the treatment of depression*
11:15 am	**Dr Jessica Vanslambrouck (Murdoch Children's Research Institute, Melbourne)** *Advances in stem cell-derived kidney organoid generation*
11:30 am	Morning Tea and Poster Presentations
Session 2	**Bio-engineering**
12:00 pm	**Dr Anita Quigley (ACES/UOW/UOM/St Vincent's Hospital Melbourne)** *Brains and Brawn: Engineering Muscle and Neural Tissues*
12:40 pm	**Dr Eva Tomaskovic-Crook (ARC Centre of Excellence for Electromaterials Science, University of Wollongong)** *Human Neural Tissues from Neural Stem Cells Using Conductive Biogel and Printed Polymer Microelectrode Arrays for 3D Electrical Stimulation*
1:05 pm	**Serena Viventi (University of Melbourne)** *Characterization of Dorsal Root Ganglia Sensory Neurons from Human Pluripotent Stem Cells and their application for developing therapies to treat Friedreich Ataxia*
1:20 pm	**Jianfeng Li (ARC Centre of Excellence for Electromaterials Science, University of Wollongong)** *Graphene Based Structures for Bone Tissue Engineering*

PROGRAM

1:35 pm	Lunch and Poster Presentations
Session 3	**Therapeutics**
1:45 pm	**Dr Serena Duchi (St Vincent's Hospital, University of Melbourne)** *Mesenchymal stem cells as multimodality therapy for osteo-chondral diseases treatment: Trojan or Work horses?*
2:25 pm	**Rachelle Balez (University of Wollongong)** *Altered distribution of alpha-tocopherol and neuroprotective effect in sporadic Alzheimer's disease induced pluripotent stem cell derived neurons*
2:40 pm	**Dr Jingjing You (Save Sight Institute, University of Sydney)** *Current clinical application of human platelet products in treating ocular diseases*
2:55 pm	**Dr Snezana Maljevic (Florey Institute of Neuroscience and Mental Health, University of Melbourne)** *Targeted therapy in neurogenetic disorders*
3:10 pm	Afternoon Tea
Session 4	**Panel Discussion** **Moderator: A/Prof Mirella Dottori (Illawarra Health and Medical Research Institute, University of Wollongong)**
3:40 pm	Lead Discussants: **Dr Michael O'Connor** **Dr Anita Quigley** **Dr Serena Duchi**
4:40 pm	Networking/close

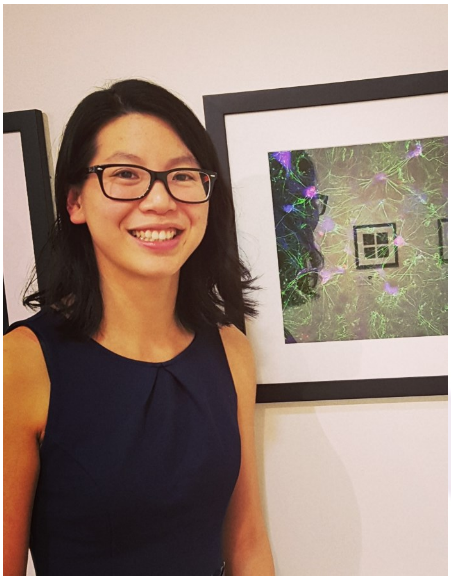
Dr Michael O'Connor—University of Western Sydney

Dr Michael O'Connor is interested in using human stem cells to better understand normal human development and disease progression. His current research uses human pluripotent stem cells (i.e. cells that can produce any cell type of the body) to learn more about the causes of - and potential new treatments for - cataract, macular degeneration and other diseases of ageing such as gut motility disorders. Michael obtained his PhD from the University of Sydney in 2005, creating an animal-based culture system that can regenerate functional ocular lenses in the laboratory. Upon completing his PhD Michael undertook postdoctoral studies in Vancouver, Canada, where he identified new genes that help maintain the developmental potential of human pluripotent stem cells. Together, these diverse areas of expertise provide a unique opportunity to understand human diseases using human cells. Throughout his career, Michael has also maintained an interest in translating academic research findings into biotechnology or clinical applications, through interactions with both Australian and Canadian biotechnology companies, and his Executive roles at the Australasian Society for Stem Cell Research.

Pursuing improved cataract treatments through pluripotent stem cell research.

Cataract, caused by opacification of the ocular lens, is one of the world's leading causes of low vision and blindness. While surgical treatment of cataract is quite effective, there is great interest in the development of anti-cataract drugs due to: i) the sheer number of cataract operations performed each year (millions); ii) the cumulative cost of these surgeries (billions of dollars); iii) the fact that, despite these surgeries, the number of people affected by cataract is increasing due to population ageing (50.5 million in 1990 to 65.2 million in 2015); and iv) the relatively high incidence of vision impairing complications that arise from cataract surgery (e.g., posterior capsule opacification). Importantly, cataract is not a single condition but rather has multiple aetiologies. Environmental factors including smoking, UV light and certain drugs (e.g., glucocorticoids) are associated with cataract formation, as are some diseases (e.g., diabetes) and a range of genetic mutations. Poor access to human lens tissue at early stages of cataract formation has meant that molecular pathologies specific to particular cataract risk factors are insufficiently understood. To address these issues, we have developed methods to generate large numbers of human lens epithelial cells and light-focusing human micro-lenses from pluripotent stem cells. This new, large-scale supply of human lens tissue is being used to define the molecular mechanisms of risk factor-specific cataract progression, to identify and test candidate anti-cataract drugs, and to investigate lens cell transplantation as a potential treatment for childhood cataract.

Dzung Do-Ha (PhD Candidate) - University of Wollongong



Dzung Do-Ha is currently a PhD candidate in her final year at the University of Wollongong and the Illawarra Health and Medical Research Institute. Under the supervision of A/Prof Lezanne Ooi, she is using iPSC-derived motor neurons and astrocytes to model amyotrophic lateral sclerosis (ALS) and investigate the underlying mechanisms which contribute to changes in neuronal excitability during the disease. Her research interests and strengths lie in developing iPSC-derived disease models, to study neuronal-glial interaction and function in neurodegenerative diseases. Moreover, she is a skilled electrophysiologist specialising in whole-cell patch clamping, one of the techniques she learned during her attendance at ACAN, a prestigious high intensity neuroscience course on electrophysiology and optical imaging.

Investigating changes in neuronal excitability using iPSC-derived motor neurons from ALS patients

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease leading to progressive paralysis. One of the earliest changes observed in patients, even prior to the deterioration of motor functions, is increased excitability of the cortical and peripheral motor neurons. The underlying mechanisms leading to changes in excitability are not yet fully understood, although it is hypothesised that intrinsic changes to ion channel function or expression in motor neurons contributes to the hyperexcitability phenotype. In this study, we generated iPSCs from an ALS-patient carrying a recently identified mutation in cyclin F CCNFS621G/WT, an enzyme involved in the ubiquitin proteasome system (UPS). We aimed to measure the effect of this mutation on the electrophysiological function of iPSC-derived motor neurons. CRISPR-Cas9 was used to generate isogenic control lines that either reversed the mutation to wildtype or created a double CCNF mutant. Subsequently we differentiated iPSCs into electrophysiologically mature motor neurons that were defined by their robust ability to fire action potentials repetitively. Whole-cell patch clamping revealed that patient-derived CCNFS621G/WT motor neurons were more excitable than the wt/wt isogenic control, whereas the excitability phenotype was exacerbated in the double mutant. These results suggest that impairments in the UPS affect ion channel function in motor neurons leading to increased neuronal excitability.

Dr Dhanisha Jhaveri—Mater Foundation, QBI, University of Queensland

Dr Dhanisha Jhaveri holds a joint appointment at Mater Research and the Queensland Brain Institute (QBI), University of Queensland and is a Mater Foundation Senior Research Fellow. She leads a research program investigating the fundamental mechanisms that drive the renewal of neurons in the adult brain, with the goal of harnessing this form of neural plasticity to relieve the emotional and cognitive burdens associated with chronic stress and neuropsychiatric disorders.

Prior to establishing her laboratory, as a Human Frontiers Science Program Long-term Fellow in Prof Perry Bartlett's laboratory, she made the seminal discovery that a subclass of clinical antidepressants directly activates quiescent neural precursor cells in the adult mouse hippocampus via a novel pathway (Jhaveri et al., J. Neurosci., 2010). This work led her to propose the presence of distinct populations of hippocampal NPCs (Jhaveri et al., Dev. Neurobiol., 2012). Funded by a previous NHMRC grant (as a CIB) she developed a new cell sorting protocol to purify hippocampal NPCs, and provided the direct evidence of distinct populations of quiescent NPCs (Jhaveri et al., J. Neurosci., 2015). Recently, she co-led the study which demonstrated that new neurons are generated in the amygdala, a key brain region for processing emotions (Jhaveri et al., Mol Psych., 2018), which is now extended through a current NHMRC Project grant.

Her group has developed and utilised a combination of innovative and multi-modal approaches including sophisticated mouse genetic models, *in vivo* lineage tracing using viral vectors, flow cytomtery, cell culture, transcriptomics, high-resolution confocal microscopy, cognitive- and mood-related behavioural tests to address these questions.

Dhanisha's research has resulted in multiple publications, successful grant funding, several awards including the Indian National Science Academy medal for Young Scientist of the Year (2003) and an Australian patent, and has led to numerous invitations to speak at national and international meetings. She is passionate about mentoring young investigators and believes that quality mentorship is vital for scientific success.

Targeting adult-born hippocampal neurons for the treatment of depression

A mechanistic understanding of how emotions are represented in the brain and lead to physiological changes that impact behaviour has been a major quest in neuroscience. Adult neurogenesis, the production and integration of new neurons in the hippocampus, has emerged as a key mechanism regulating the hippocampal circuitry and a vital player in the modulation of cognition and emotion. However, precise roles of adult-born neurons in regulating the local circuitry and mediating behavioural responses to stress and antidepressants are not fully understood. In this talk, I will present our recent data showing that genetic ablation of adult-born neurons during a critical window of neuronal maturation prevents chronic stress-induced anxiety. I will further discuss our *ex vivo* electrophysiology findings combined with morphological analyses that demonstrate selective alterations in membrane properties, maturation status and local connectivity of these adult-born neurons in stressed animals and show that these changes are reversible by treatment with a select clinical antidepressant. These results provide evidence for an instructive role of adult-born, immature hippocampal neurons in regulating stress-induced changes in the local hippocampal circuitry and depression-related behaviours and suggest that interventions that target the properties of these adult-born neurons may prove useful for treating these core symptoms of depression.

Dr Jessica Vanslambrouck—Murdoch Children's Research Institute, Melb

Dr Jessica Vanslambrouck is currently a Research Officer in the Kidney Development, Disease and Regeneration Group led by Professor Melissa Little (Murdoch Children's Research Institute, Melbourne), with her research career over the last 10 years focussing on kidney physiology, disease and regeneration. During her PhD in the group of Professor John Rasko (Centenary Institute, Sydney), Dr Vanslambrouck elucidated the expression of several renal amino acid transporters during development and disease, while establishing a connection between transporter expression and transplant rejection. Her passion for this research and strong interest in regenerative medicine led her to accept a postdoctoral position in Professor Little's Kidney Research group (formerly in the Institute for Molecular Bioscience, Queensland), world-leaders in the fields of kidney development and renal stem cells. Her postdoctoral studies have primarily involved the investigation of regenerative options for chronic kidney disease through re-creation of the transient embryonic kidney stem cell (nephron progenitor) population present during development. This research has contributed to the first reports of both direct reprogramming to nephron progenitors and directed differentiation of pluripotent stem cells to complex 'mini-kidney' organoids. More recently, Dr Vanslambrouck's focus on kidney organoids has expanded to include overall improvement of organoid development and maturation.

Advances in stem cell-derived kidney organoid generation

Progress in the fields of stem cell differentiation and organoid generation hold great promise for regenerative medicine, disease modelling and drug screening. Based on our knowledge of human kidney development, we have established a robust protocol to direct the differentiation of human induced pluripotent stem cells (iPSCs) towards kidney cell types capable of forming complex 3D kidney organoids (Takasato et al., 2016). These organoids display evidence of differentiation into many of the compartments present in early embryonic kidney, including nephrons, collecting duct, vasculature and interstitium. However, despite this exciting progress, organoids do not yet fully recapitulate the cellular maturity and structural complexity of human kidneys *in vivo*. Through the application of novel tools and techniques such as kidney cell type-specific iPSC reporter lines and 3D cellular bioprinting, we are gaining a deeper insight into organoid morphogenesis and more precise control over patterning via the manipulation of culture format, media conditions and the biophysical properties of organoids themselves. Further research into the variables of organoid generation will be fundamental to achieve and maximise their future downstream applications in the kidney development and disease fields.

Dr Anita Quigley - ACES/UOW/UOM St Vincent's Hospital Melbourne

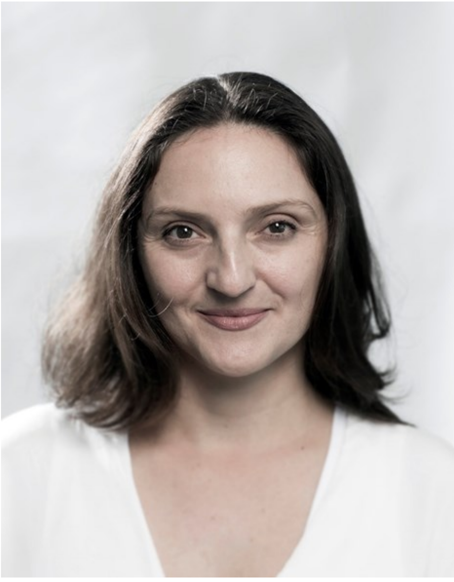
Dr. Anita Quigley completed a PhD at the Department of Medicine, Melbourne University with a focus on mitochondrial function in end stage cardiomyopathies. She is currently a Research Fellow at the University of Wollongong as part of an ARC Centre of Excellence and a Honorary Fellow at the Department of Medicine, University of Melbourne. She is currently located at the new flagship BioFab3D@ACMD laboratories and Department of Clinical Neurosciences at St. Vincent's Hospital Melbourne and will be commencing a Vice Chancellor's Senior Research Fellowship with RMIT in July 2019.

Her current activities involve the use of human iPSC for modelling neurological disorders, the development of anti-fouling electrodes and surfaces for bionic devices, biomaterials for neural engineering, 3D bioprinting, the delivery of stem and progenitor cells to neural and muscle tissues and the differentiation of iPSC to neural and muscle lineages. Her work involves multi-disciplinary liaison with collaborators from diverse fields including neuro and orthopedic surgery, textile fabrication technology, chemistry and material science. She has co-supervised 16 PHD, Masters and Honours students through to completion at the University of Melbourne and University of Wollongong and has over 70 peer reviewed publications and book chapters in molecular biology, medical and materials science journals.

Brains and Brawn: Engineering Muscle and Neural Tissues.

There is a growing movement in cell biology where researchers are moving away from 2D tissue culture systems to 3D culture, particularly in the areas of tissue engineering, neuroscience and cancer research. Our laboratories are focusing on the use of bioengineering methods, including bioprinting and 3D culture, for tissue engineering as well as for the study of neurological disorders. We have shown that 3D primary neural cultures demonstrate different neural network activity than 2D cultures, with activity in 3D showing more "brain like" behavior. We are currently developing these methods for the assessment of neurological disorders using iPSC stem cells derived from patients with neurological disorders. We are also using 3D bioengineering techniques for the creation of vascularized 3D skeletal muscle constructs for tissue engineering as well as the delivery of muscle progenitor cells to skeletal muscle. We have employed various fabrication techniques to achieve this, including 3D bioprinting, and have successfully achieved enhanced myogenic progenitor delivery to skeletal muscle and created de-novo muscle for repair of volumetric muscle defects in animal models.

Dr Eva Tomaskovic-Crook—ACES, University of Wollongong



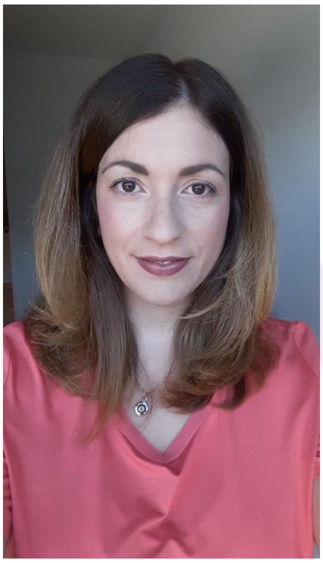
Dr Eva Tomaskovic-Crook is a Research Fellow within the Synthetic Biosystems program of the ARC Centre of Excellence for Electromaterials Science (ACES) at the University of Wollongong. Her current research focus is to interface human stem cells and neural tissue derivatives with cell instructive biomaterials and electromaterials for the production of novel 3D synthetic biosystems for research and translational applications, including drug/toxicity screening, stem cell based therapies, disease diagnostics and medical device development.

Before joining ACES, Eva completed her PhD with the University of Melbourne at the Ludwig Institute of Cancer Research where she investigated in vitro cellular mechanisms of antibody-mediated delivery of nanoparticles to colorectal cancer cells for targeted immunotherapy. Following her PhD, Eva undertook a post-doc in Singapore with A*STAR's Institute of Molecular and Cell Biology and at St Vincent's Institute in Melbourne, Australia. Her research applied bioinformatic approaches to identify novel therapeutic targets altered in molecular subtypes of breast cancer. Prior to her PhD, Eva worked in the fields of Schizophrenia neurobiology and therapeutic drug research and development, at the Mental Health Research Institute of Victoria and at the Clinical Brain Disorders Branch of the National Institute of Mental Health at the US National Institutes of Health.

Human Neural Tissues from Neural Stem Cells Using Conductive Biogel and Printed Polymer Microelectrode Arrays for 3D Electrical Stimulation

Electricity is important in the physiology and development of human tissues such as embryonic and fetal development, and tissue regeneration for wound healing. Accordingly, electrical stimulation (ES) is increasingly being applied to influence cell behaviour and function for a biomimetic approach to *in vitro* cell culture and tissue engineering. Here we describe the application of conductive polymer (CP) poly(3,4-ethylenedioxythiophene)-polystyrenesulfonate (PEDOT:PSS) pillars, direct-write printed in an array format, for three-dimensional (3D) ES of maturing neural tissues that are derived from human neural stem cells (NSCs). NSCs are initially encapsulated within a conductive polysaccharide-based biogel interfaced with the CP pillar (microelectrode) arrays (MEAs), followed by differentiation *in situ* to neurons and supporting neuroglia during stimulation. Electrochemical properties of the pillar electrodes and the biogel support their electrical performance. Remarkably, stimulated constructs are characterised by widespread tracts of high-density mature neurons and enhanced maturation of functional neural networks. Formation of tissues using the 3D MEAs substantiates the platform for advanced clinically-relevant neural tissue induction, with the system likely amendable to diverse cell types to create other neural and non-neural tissues. The platform may be useful for both research and translation, including modelling tissue development, function and dysfunction, electroceuticals, drug screening and regenerative medicine. (Tomaskovic-Crook E, et al. Advanced Healthcare Materials (in press).)

Serena Viventi (PhD Candidate) - University of Melbourne



Serena Viventi is a PhD candidate at the Biomedical Engineering Department (The University of Melbourne). In 2013, she completed a master's degree in Neuroscience at the University of Trieste, Italy. Her previous studies investigated the effect of human umbilical cord mesenchymal stem cells and human neural stem cells in a mouse model of Amyotrophic Lateral Sclerosis after transplantation. Her interest in stem cells brought her to Melbourne for her PhD project, focused on the differentiation of hPSC-derived sensory neurons, cell replacement and gene delivery nanoparticles-mediated for treating peripheral neuropathies. Her studies will provide new insights for using hPSC as a model to study human DRG development, phenotypic and functional properties of human sensory neuronal subtypes and for evaluating advanced alternative therapies to treat DRG sensory-related disorders, particularly Friedreich Ataxia.

Characterization of Dorsal Root Ganglia Sensory Neurons from Human Pluripotent Stem Cells and their application for developing therapies to treat Friedreich Ataxia

FRDA is an autosomal recessive disease characterized by degeneration of DRG proprioceptive sensory neurons, which is due to a low level of the mitochondrial protein Frataxin (FXN). Having an in vitro source of human DRG sensory neurons, such as from human pluripotent stem cells (hPSC), is paramount for studying their development, unique neuronal properties and for accelerating regenerative therapies to treat sensory neuropathies, including FRDA.

Part of my studies interrogated the ability of hPSC-derived sensory neurons to survive, differentiate and integrate in vivo. Transplantations of hPSC-derived sensory neural progenitors, both from hESCs and FRDA iPSCs, were performed in the DRG of adult rats and tissue analyses were performed at 2-8 weeks post-transplantation. Our results showed survival of transplanted donor cells, within and surrounding the DRG and, most importantly, donor cells expressed markers of DRG sensory neurons and glia, demonstrating their capacity to differentiate to sensory neuronal and glial lineages in vivo. These novel studies start to address the possibility of developing cell replacement therapies for treating neurodegeneration occurring within the peripheral sensory nervous system, particularly in FRDA. In addition, we explored the therapeutic application of nanoparticles to deliver Frataxin-expression plasmid into hPSC and FRDA iPSC-derived sensory neurons. We tested several nanoparticle types that varied in their composition properties, sizes and charge to identify the most effective nanoparticles that are capable of being taken up by sensory neurons and deliver plasmid. Our preliminary results were promising for showing potential therapeutic use of nanoparticles as delivery system.

In conclusion, our data provide new insights for using hPSC as a model to evaluate advanced alternative therapies to treat DRG sensory-related disorders, particularly FRDA.

Jianfeng Li (PhD Candidate) - University of Wollongong

Jianfeng Li is a final year PhD student from University of Wollongong. His PhD project is focused upon fabrication of 3D graphene based scaffolds and application of the scaffolds towards tissue regeneration. During his PhD, he has developed a series of graphene based scaffolds, which are suitable for human stem cell and tissue support. Various fabrication strategies have been utilized in his project, like salt leaching, dip coating, origami and 3D printing. The as-fabricated graphene scaffolds can be applied in either 2D or 3D graphene based electrical stimulation device development, and applied electrical stimulation via the devices was found capable of enhancing stem cell activity. Jianfeng obtained his bachelor degree in Pharmaceuticals from China and master degree in Bionano from South Korea, during which he has developed several efficient DNA sensing platforms. Prior to starting his PhD, he worked as a research assistant on development of wearable device at The Hong Kong Polytechnic University.

Graphene Based Structures for Bone Tissue Engineering

Autograft, as "gold standard" in orthopaedic surgery, is almost unable to meet the growing demand for bone transplantation due to global aging and obesity issues. This urgent need of available bone grafts has driven the development of tissue engineered bone implants forward to meet the request. Graphene based materials have attracted enormous interest towards osteogenic restoration or reconstruction in bone tissue engineering due to the extraordinarily versatile properties of graphene. Meanwhile, biophysical stimulating factors, especially electrical stimulation (ES) factor, are found capable of encouraging osteogenic regeneration via upregulation of extracellular matrix protein synthesis and enhancement of cellular repair. However, current widely used electrodes for ES are mostly metal-based, suffering from being corrosive and high destructive voltage derived from its very low electrical resistance. Here, anti-corrosive conductive graphene scaffold and electrical stimulation are combined to address these challenges for bone regeneration. To achieve this, robust, biocompatible and electrically conductive graphene-cellulose (G-C) paper was developed, and an efficient, miniaturized G-C paper-based electrical stimulation device for bone tissue engineering was fabricated. Coupling the electrical stimulating signals with superior graphene intrinsic properties, this device can significantly enhance the proliferation and osteogenic differentiation of human adipose derived stem cells (ADSCs), which supports the beneficial use of ES delivered through graphene based scaffold for bone regeneration.

Dr Serena Duchi— St Vincent's Hospital, Melbourne

Dr. Serena Duchi is a cellular biologist with special interest in osteochondral tissue engineering.

She graduated in Biology in 2004 (University of Bologna, Italy), she obtained a Master degree in Bioinformatics in 2005 at the Centro de Investigación Príncipe Felipe (CIPF) Valencia – Spain. She then obtained her PhD in Cell, Molecular and Industrial Biology in 2009 through an international program between University of Bologna-Italy and Medical University of South Carolina (MUSC), Hollings Cancer Center, Charleston, SC-USA, with a thesis in tumor cell biology and endocytosis mechanisms in in vitro and in vivo models. She was awarded a post-doctoral fellowship at the IFOM-FIRC Institute of Molecular Oncology, Milan-Italy in 2009, where she acquired a strong background in the regulation of tumor suppression and endocytosis aimed to design new molecular target chemotherapeutic drugs. She then specialized in the treatment of musculoskeletal tumors at the Rizzoli Orthopaedics Institute, Bologna-Italy, where she led as senior investigator different projects:

• safety of mesenchymal stem/stromal cells (MSC) isolated and expanded from osteosarcoma and healthy subjects; • use of MSC for drug delivery as innovative therapeutic approach for the treatment of osteosarcoma; • use of MSC in scaffold based regenerative medicine for osteo-chondral defect and diseases treatments. Dr. Duchi moved to Melbourne in April 2016 as an academic research fellow and she's currently working at the St Vincent's Hospital, 3DBioFab facility @ ACMD, in the cartilage regeneration team led by Prof. Peter Choong and Dr. Claudia Di Bella. The project is centred on the use of advanced 3D printing technologies for the regeneration of healthy articular cartilage both in vitro and in vivo. She is specialized in:• human stem cells isolation, characterizations and differentiation in osteochondral lineage;• 3D bioprinting and cultivation of samples for cartilage tissue regeneration;

• imaging techniques for epifluorescence, confocal and time-lapse microscopy, FRET, TIRF, Light-Sheet Microscopy.

Mesenchymal stem cells as multimodality therapy for osteo-chondral diseases treatment: Trojan or Work horses?

Since many years research and usage of adult mesenchymal stem/stromal cells (MSCs) represent one of the most exciting fields in cell-based therapy. Their safety and efficacy have been reported in > 250 clinical trials (Kramer J, Dazzi F, Dominici M, Schlenke P, Wagner W. Clinical perspectives of mesenchymal stem cells. Stem Cells Int. 2012;2012:684827). MSCs are appealing because they can be easily isolated from bone marrow and several other human tissues and they can be safely expanded *in vitro. They display* high proliferative capacity, low immunogenicity, immunomodulatory properties, and they have the ability to secrete soluble factors that regulate crucial biological functions, such as proliferation and differentiation over a broad spectrum of target cells. These features render them a very unique tool as targetable vehicles to deliver therapeutic drugs to the tumor stroma. In addition, the ability of MSCs to differentiate into several cell lineages makes them ideal for reparative medicine. Thanks to these characteristics, MSCs are the elective cells that can act as Trojan-horses to deliver chemoterapuetics drugs to kill bone derived sarcoma, or act as Work-horses by behaving as the building blocks in articular cartilage biofabrication approaches. In this talk I will discuss about the focus of my research on the therapeutic usage of MSCs as multimodal therapy to treat osteosarcoma and rebuild compromised cartilage to prevent osteoarthritis.

Rachelle Balez (PhD Candidate) - University of Wollongong

Rachelle Balez is a final year PhD candidate at the Illawarra Health and Medical Research Institute, University of Wollongong, under the supervision of A/ Prof Lezanne Ooi. Rachelle's research focuses on the generation of patient-derived iPSCs and neurons as a platform for neurodegenerative disease modelling. Using this disease platform, Rachelle investigates alterations to the lipid membrane and calcium signaling pathways in the context of oxidative and nitrosative stress insult during Alzheimer's disease. Rachelle has a particular interest in molecular imaging and has conducted research at the Maastricht Multi Modal Molecular Imaging Institute in the Netherlands. Beyond research, Rachelle is driven to promote diversity and equality in STEMM and has held the role of student representative on the national council for the Australasian Neuroscience Society and is an alumna of Homeward Bound, a global women in science leadership initiative.

Altered distribution of alpha-tocopherol and its potential neuroprotective effect in induced pluripotent stem cell derived neurons from Alzheimer's disease patients.

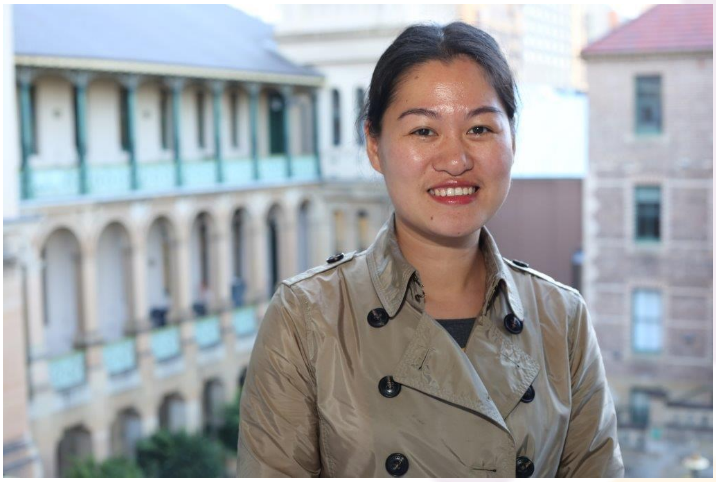
Late-onset Alzheimer's disease (LOAD) is the most common neurodegenerative disorder and is characterised by amyloid plaques and neurofibrillary tangles. Early pathogenic changes in the AD brain also include alterations to the composition of lipid membranes and elevated levels of oxidative stress markers. Clinical trials indicate that alpha-tocopherol (α-toc), a lipid soluble antioxidant, may be protective during early stages of cognitive decline in AD, however little is known regarding the distribution and neuroprotective action of α-toc in living human neurons.

Using induced pluripotent stem cell (iPSC) derived neurons, the aim of this study was to image the distribution of α-toc in the lipid membrane of neurons and determine the effect of α-toc treatment on neurite length and markers of oxidative and nitrosative stress.

The iPSCs were generated from the fibroblasts of AD patients and non-AD controls and differentiated into neurons. Simultaneous tandem time-of-flight secondary ion mass spectrometry imaging was used to visualise the lipidome of neurons, identifying a peak at m/z 430 as α-toc. In addition, the effect of α-toc treatment on neurite length and markers of oxidative and nitrosative stress was determined.

The distribution of α-toc was restricted to the soma in AD neurons, while in control neurons it was localised in the neurites and soma. Neurite length in AD neurons was significantly reduced in comparison to control neurons, with α-toc treatment for 7 days increasing neurite length in both AD and control neurons. In addition, α-toc treatment significantly reduced the level of peroxidation and nitrite, markers of oxidative and nitrosative stress, respectively, in sAD neurons. Taken together, the restricted distribution of α-toc to the soma of AD neurons in conjunction with reduced neurite length could indicate that these neurites have increased susceptibility to lipid peroxidation and oxidative stress, with modulation of α-toc levels able to restore some protection. Collectively our results imply that α-toc may be neuroprotective against aspects of AD pathology and warrants further investigation.

Dr Jingjing You—Save Sight Institute, University of Sydney



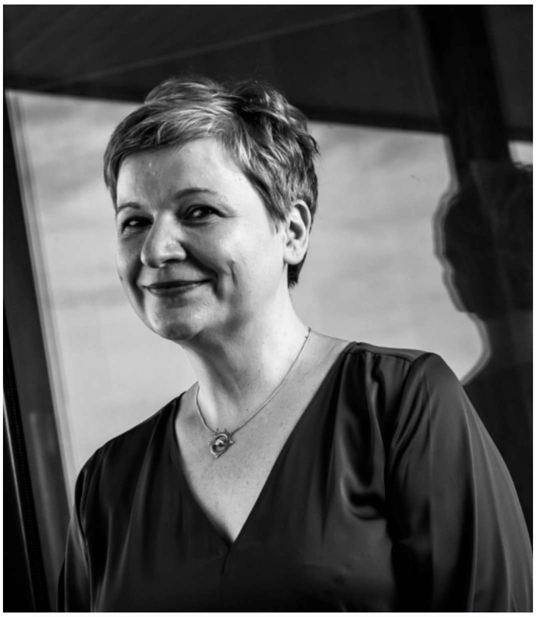
Dr Jingjing You is a postdoctoral research fellow and the lead scientist of laboratory research team, corneal bioengineering group at Save Sight Institute, University of Sydney; a visiting Academic at School of Optometry and Vision Science (SOVS), UNSW Sydney; an external scientific advisor for NSW Tissue Bank, South Eastern Sydney Local Health District and a working committee member of Australian/New Zealand Human Eye Cell Atlas Consortium.

She has published over 20 papers, granted 1 provisional patent and generated the first public gene database for corneal epithelium cells (GEO dataset ID: GSE112155). Her current research focus is on corneal bioengineering and the development of biomaterials to optimise corneal regeneration. Her research has led to the development of iFix^{TM} system and funding from 2018 NSW Medical Device Fund for commercialisation. She is the co-founder and working committee member of Australia Corneal Bioengineering Working Group, and a regular speaker for the annual 3D printing workshop organised by University of Wollongong and University of Melbourne.

Current clinical application of human platelet products in treating ocular diseases

Human platelets have been found to play an important role beyond hematological diseases. Use of platelets and their relevant products in clinics has been extended to skin, muscle, joint, stem cell and ophthalmic treatments. Studies have reported use of platelet rich plasma, human platelet lysate, plasma rich in growth factors and platelet gel in treating ocular diseases such as dry eye disease, and corneal ulceration. However, there is a large variation between the method used to generate platelets and their related products, leading to difficulties in comparing their clinical effects. This presentation focuses on the role of various platelet products in ophthalmic clinics, including platelet rich plasma, human plate lysate, platelet rich growth factors and platelet gels, and the challenges faced by using platelet products in clinics. It will also present data on using human platelet lysate to culture corneal epithelial, stromal and endothelial cells and its potential on cell therapies.

Dr Snezana Maljevic—The Florey Institute, University of Melbourne



Dr. Snezana Maljevic heads the Functional Epilepsy Genomics Laboratory at the Florey Institute of Neuroscience and Mental Health in Melbourne. She is a disease biologist with a recognised expertise in functional genomics of genetic epilepsy. Dr. Maljevic earned her Master's degree in Molecular biology and Physiology at the University of Belgrade in Serbia. She then moved to Germany where she completed her PhD and postdoctoral training in one of the European leading labs in the field of epilepsy genetics and has made significant contributions to the understanding of the genetic and functional basis of epileptic and neurodevelopmental disorders. She has played major roles in European genetic epilepsy initiatives and was recruited three years ago to the Ion Channels and Human Disease group led by Prof Steven Petrou at the Florey Institute. Her current work aims at the development of precision medicine approaches for the treatment of severe epilepsies.

Targeted therapy in neurogenetic disorders

Developmental and epileptic encephalopathies (DEE) are group of neurogenetic disorders characterised by severe epilepsy and developmental delay. Affected children have ongoing seizures, cognitive impairment, movement disorders and overall poor prognosis. Only ten years ago, there were no known causes of DEE and little hope could be offered to patients and their families. However, with the breakthrough of next generation sequencing technology genetic causes of the disease, including a myriad of mostly de novo and mosaic variants, have been identified in affected children. These variants are found in >50 genes and currently account for about 30 % of DEE cases. We have established in the recent years one of the largest repositories of fibroblasts obtained from DEE patients with the aim to generate and analyse induced pluripotent stem cell (iPSC)-derived neuronal models. The talk will focus on the characterisation of the iPSC neuronal models of DEE caused by variants in two genes critical for the regulation of neuronal excitability, KCNQ2 and SCN2A. Two different neural differentiation approaches were used to generate these models, including a 'fast' protocol based on NGN2 overexpression, and a more 'native' embryoid body protocol. The analysis included patch clamp and multielectrode array recordings to assess changes in neuronal excitability. We will look into how the identified disease mechanisms can help develop targeted treatments for these disorders.

Posters

Generation of Vestibular Tissue-Like Organoids from Human Pluripotent Stem Cells using the Rotary Cell Culture System

Cristiana Mattei1,2, Rebecca Lim3, Hannah Drury3, Babak Nasr1,4,5, Zihui Li2, Melissa A. Tadros3, Giovanna M. D'Abaco2, Kathryn S. Stok2, Bryony A. Nayagam6 and Mirella Dottori1,2,7*

1 Centre for Neural Engineering, Melbourne School of Engineering, The University of Melbourne, Melbourne, VIC, Australia, 2 Department of Biomedical Engineering, Melbourne School of Engineering, The University of Melbourne, Melbourne, VIC,Australia, 3 School of Biomedical Sciences and Pharmacy, Faculty of Health and Medicine, University of Newcastle, Newcastle, NSW, Australia, 4 Department of Electrical and Electronic Engineering, Melbourne School of Engineering, The University of Melbourne, Melbourne, VIC, Australia, 5 ARC Centre of Excellence for Integrative Brain Function, The University of Melbourne, Melbourne, VIC, Australia, 6 Departments of Audiology and Speech Pathology and Department of Medical Bionics, The University of Melbourne, Melbourne, VIC, Australia, 7 Illawarra Health and Medical Research Institute, The University of Wollongong, Wollongong, NSW, Australia.

Interrogating the mechanism underlying cognitive impairments in Type 1 diabetes using human embryonic stem stems

Michal Mor 1, 2, Fergus Cameron 3, Mary Familari 4, Gursharan Chana 1, 5,Alexandra Harvey 4 and Mirella Dottori 1,2, 6, 7

1 Centre for Neural Engineering, University of Melbourne, Australia.2 Department of Anatomy, University of Melbourne, Australia. 3 Murdoch Children's Research Institute, The Royal Children's Hospital, Australia.4 School of BioSciences, University of Melbourne, Australia.5 Department of Medicine (Royal Melbourne Hospital), University of Melbourne, Australia.6 Department of Biomedical Engineering, University of Melbourne, Australia.7 Illawarra Health and Medical Research Institute, University of Wollongong, Australia.

Expression profiling of REST and RCOR genes in neurogenesis using human embryonic stem cells

Simon Maksour
Illawarra Health and Medical Research Institute, The University of Wollongong, Wollongong, NSW, Australia.

Notes

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The NSW Stem Cell Network is a professional community with an interest in all forms of stem cells.

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