MONASH University

MONASH
MEDICINE, NURSING
AND HEALTH SCIENCES

2019 CCS 12th ANNUAL

GRADUATE RESEARCH SYMPOSIUM

OF THE STUDENTS, BY THE STUDENTS, AND FOR THE STUDENTS

Monday 7th October, 2019

https://www.monash.edu/medicine/ccs/education/current-students/hdr-symposium

Cover image: 2018 CCS Graduate Research Symposium

Booklet compiled by Muthu Mohan

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Introduction

Date: 7-Oct-2019 (Monday)
Venue: Lecture Theatre, Level 5, Alfred Centre

The main aim of the Central Clinical School's (CCS) symposium is to improve the visibility of students and their research projects on a larger scale and celebrate their achievements.

This symposium gives an opportunity for students to explain their research to other students and enables fostering of collaborations, networking and a greater awareness of the expertise and research being conducted on the site.

This is a student run event. The 2019 Postgraduate symposium planning committee members are:





Chair:

Mr. Muthu Mohan	Ms. Lakshanie Wickramasinghe	Mr. Rishabh Sharma	Ms. Akshita Rana	Ms. April Raftery
Diabetes	*Immunology & Pathology*	*Neuroscience*	*ACBD*	*Immunology & Pathology*

Student oral and poster presentations will be judged by a panel of senior academics and postdocs, with monetary prizes given for outstanding work.

Prizes for outstanding work

Most outstanding oral presentation	**$400**
Most outstanding poster presentation	**$400**
Second place oral presentation	**$200**
Second place poster presentation	**$200**
Third prize oral presentation	**$100**
Third prize poster presentation	**$100**
People's choice (oral presentation)	**$50**
Student raffle prize*	**$50**

*Raffle tickets will be issued to students who ask questions (1 ticket per question). So, the more questions, the higher chance of winning!

2018 CCS GR symposium committee

Chair:
Mr Paul Gill

Gastroenterology

Ms Minhee Halemba

ACBD

Ms Lakshanie Wickramasinghe

Immunology & Pathology

Ms Angela Nguyen

Immunology & Pathology

Mr Daniel So

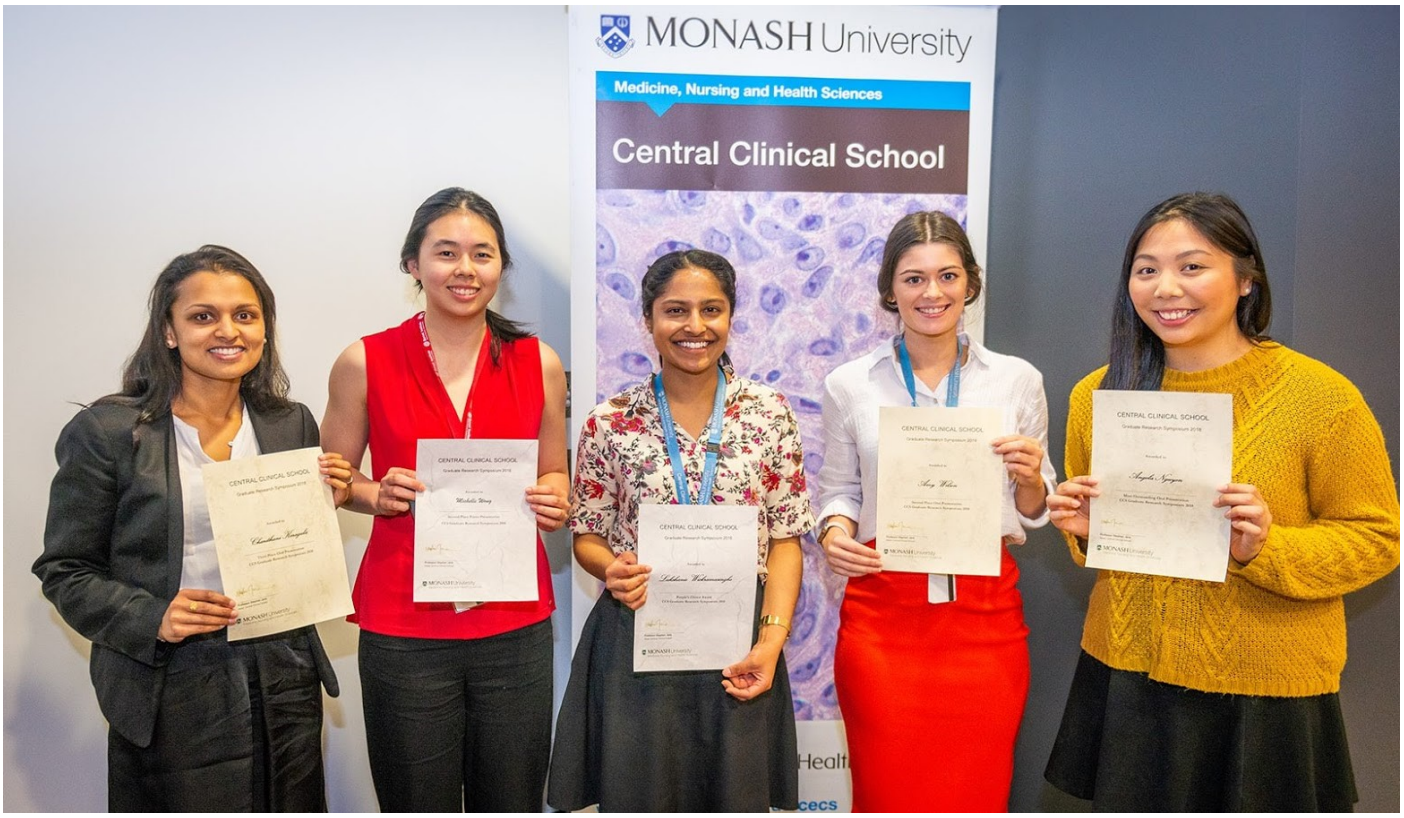
Gastroenterology

Ms Ee Fang Yu

Baker Institute

Organising committee for the 2018 Central Clinical School 11th annual Graduate Research symposium held in the Alfred Centre.
L-R: Mr Paul Gill, Ms Minhee Halemba, Ms. Lakshanie Wickramasinghe, Ms. Angela Nguyen, Mr. Daniel So, Ms. Ee Fang Yu

2018 CCS GR symposium winners



L-R: 2018 CCS Graduate Research symposium winners Charithani Keragala, Michelle Wong (runner up, poster presentation), Lakshanie Wickramasinghe, Amy Wilson, Angela Nguyen (winner, oral presentation) 2018 Central Clinical School 11th annual Graduate Research symposium held in the Alfred Centre

Program

Monday 7th October, 2019

10:10-10:20 am	**Introduction & Welcome: Mr. Muthu Mohan, Chair student committee**
Session 1: Oral presentation **Chair: Ms. April Raftery**	
10:20-10:30 am	Speaker: Mr. Hattapark (Jeff) Dejakaisaya
10:30-10:40 am	Speaker: Mr. Paul Gill
10:40-10:50 pm	Speaker: Mr. Feng Yan
10:50-11:00 am	Speaker: Dr. Mahima Kapoor
11:00-11:10 am	Speaker: Mr. Robert Cooper
11:10-11:20 am	Speaker: Ms. Anna Harutyunyan
Session 2: Explain my graph **Chair: Ms. Akshita Rana**	
11:30-12:00 pm	**Participants**: Prof. Terence O'Brien (Neuroscience) Prof. Nicola Harris (Immunology) Prof. Helmut Butzkueven (Neuroscience) **Judges:** Committee
12:00-1:10 pm	**Lunch accompanying poster display (as listed under Session 3 below)**
Session 3: Poster presentations **Venue: Seminar Room 2, Level 5, Alfred Centre** **Chair: Ms. April Raftery and Mr. Rishabh Sharma**	
(01)	Presenter: Ms. Erica Plummer
(02)	Presenter: Ms. Sarah Griffith
(03)	Presenter: Ms. Georgia Symons
(04)	Presenter: Ms. Nicola Sergienko
(05)	Presenter: Mr. Xianglong Xu
(06)	Presenter: Mr. William O'Brien
(07)	Presenter: Ms. Alexandra Dimitropoulos
(08)	Presenter: Ms. April Raftery
(09)	Presenter: Mr. Muthu Mohan

Session 4: Oral presentation **Chair: Mr. Muthu Mohan**	
1:10-1:20 pm	Speaker: Mr. Rishabh Sharma
1:20-1:30 pm	Speaker: Ms. Rosie Latimer
1:30-1:40 pm	Speaker: Ms. Lakshanie Wickramasinghe
1:40-1:50 pm	Speaker: Mr. Ryan Wick
1:50-2:00 pm	Speaker: Dr. Robb Wesselingh
2:00-2:10 pm	Speaker: Mr. Wei Yeh

Session 5: No-Bell Prize **Chair: Ms. Lakshanie Wickramasinghe and Mr. Muthu Mohan**	
2:10-2:40 pm	**Participants**: Prof. Benjamin Marsland (Immunology) Prof. Jayashri Kulkarni (MAPrc) Prof. Mark Cooper (Diabetes) **Judges:** Committee **Timekeeper:** Ms. Akshita Rana
2:40-2:45 pm	Representative from MPA
2.45-3.00 pm	**Closing remarks and awarding of Prizes**
3:00 pm	**Networking afternoon tea**

Judges for events

Judges for Oral presentations (session 1)

Chair:
Ms. April Raftery

A/Prof. Ross Dickins

Prof. Sam El-osta

A/Prof. Catriona Bradshaw

Judges for Poster presentations (session 3)

Chair:
Ms. April Raftery

Chair:
Mr. Rishabh Sharma

Prof. Nicola Harris

Prof. Helmut Butzkueven

Judges for Oral presentations (session 4)

Chair:
Mr. Muthu Mohan

Dr. Bridgette Semple

A/Prof. Eric Chow

Prof. Raffi Gugasyan

Supervisor session

No-Bell prize

Watch supervisors explain their complicated research without using any technical language! See how long they can go without ringing the bell. The interviewee who uses the least number of jargon words wins the session and a prize.

L-R: Prof Benjamin Marsland explaining significance of colour of cattle leading to obesity and Head of School, Prof Stephen Jane awarding 2018 CCS Explain my graph winner, Prof. Peter Gibson

Explain my graph

Supervisors are given 3-4 data and summary slides from outside their specialty area and have to present the slides to the audience. Each speaker has 5 minutes to present the slides followed by 2 minutes of questions from the audience. The best presenter wins the session and a prize.

L-R: Prof Stephen Jane presenting 2018 CCS No-bell prize award to A/Prof. Mark Wright and Prof. Nicola Harris participating in the event

Oral presentation

Mr. Hattapark (Jeff) Dejakaisaya
Neuroscience

Title: *The role of glutamate in the pathogenesis of acquired epilepsy in Alzheimer's Disease*

Alzheimer's disease (AD) can increase the risk of epileptogenesis up to 10-fold in patients, compared to healthy age-matched controls. However, the underlying mechanisms leading to this increased risk have not been discovered.
AIMS & HYPOTHESIS: Here we proposed that changes in the brain occurring early in the AD disease process contribute to a susceptibility to epileptogenesis. Early disruption in the brain's glutamate homeostasis has been reported in both epilepsy and AD and therefore this study aimed to explore the potential role of glutamate in the pathogenesis of acquired epilepsy in AD. It also aimed to identify potential early biomarkers for acquired epilepsy in AD.
METHODS: Brain tissue was excised from 6 month-old Tg2576 AD mice along with their wild-type (WT) littermate. Western blotting and mass spectrometry were performed on the extracted brain samples. RESULTS: Tg2576 mice had significantly lower amounts of GLT-1 and Glutamine synthetase in the cortex, compared to the WT ($p<0.01$). Results from Mass spectrometry have shown that metabolites such as glutamate and glutamine have the potential to be the early biomarkers for acquired epilepsy in AD. CONCLUSION: The results show disruptions to the glutamate-glutamine cycle in Tg2576 mice, suggestive of impairment in astrocytic function. These findings support the hypothesis that the brain's glutamate homeostasis is affected early in AD and that this might lead to a higher susceptibility of the brain to epileptogenesis via the extracellular glutamate spill-over in the synaptic cleft. The findings from the metabolomics analysis also suggest that there are changes in different brain's metabolites early in AD.

Mr. Paul Gill
Gastroenterology/Immunology

Title: *Dietary intervention that increases exposure to short chain fatty acids (SCFA) alters the phenotypic patterns of adaptive immune cells in healthy humans*

Immune-modulating effects of SCFA in animal disease models have not been demonstrated in humans.
The aim of this study was to determine whether increased exposure to SCFA via dietary manipulation previously shown to increase colonic and systemic delivery of SCFA modulates the phenotypic patterns of peripheral blood immune cells.
Healthy subjects (n=20) underwent a blinded, randomized dietary intervention, consuming for 21 days a high SCFA-producing diet, containing 38 g/day total fibre (incl 10 g resistant starch and 8 g inulin) with 20 mL apple cider vinegar 3 times/day, or matched placebo diet, containing 20 g/day fibre with pH-matched apple juice drink, with 21-day wash-out between. Blood and 3-day total faecal output were collected at baseline and in each dietary period.
Preliminary results show that median total faecal SCFA concentration (measured by gas chromatography) was greater in the high- than low- SCFA diet (92.0 vs 112.8 umol/g; n=17; p=0.08). Immunophenotyping of blood cells (flow cytometry) in 17 subjects revealed lower median frequency of B-cells (173 vs 199 cells/µL, p=0.02) and CD8+ T-cells (491 vs 574 cells/µL, p=0.09) after the high- vs low-SCFA diet.
Greater exposure to SCFA over 21 days via dietary manipulation modulates the distribution of adaptive immune cells, a novel function for SCFA in human health. Further immune-phenotyping and blood plasma SCFA analysis is ongoing to investigate mechanism of action for these findings.

Mr. Feng Yan
ACBD

Title: *Unveiling a Distinct Signature in Leukemia Stem Cells using Multi-omics data*

Background: B cell Acute Lymphoblastic leukemia (B-ALL) is the most common cancer in children. Although the 5-year overall survival rate is around 85%, there are still 20% patient succumb to relapse. The cytogenetics is complex in B-ALL and around 30% patients carry unknown cytogenetics. Leukemia stem cells (LSC) are a rare population in leukemia, which are believed to cause relapse after conventional treatment. We aim to use LSC gene signature to develop an easy way to predict patient risk at diagnosis. Methods: Publicly available LSC RNA-seq for B-ALL was obtained from GEO and analysed using RNAsik and edgeR. Training data including patient RNA-seq expression matrix and clinical information was obtained directly from TARGET website. Test datasets were microarray from GEO and TARGET website including clinical information. LASSO regression was done on training data with 10 folds cross validation (CV) using different input features. CV was done 100 times randomly for each input to select top 3 models with most occurrence. All models generated were then tested in all three test datasets to validate the power of risk prediction based on hazard ratio and p value. Survival analysis was based on Cox model. Result: Differential expression genes from LSCs were enriched in pathways related to immune response (MHC family), cell cycle arrest. Genes upregulated in LSCs with significant adverse survival impact were selected for LASSO regression. The final model is 0.065*S100A10+0.051*ZMAT3+0.017*PSAT1+0.108*RIMS3+0.01*LRRC25+0.015*H1FX+0.04*TSPO+0.029*NID2+0.014*CCDC69. It showed superior predictive power in all three test data including 2 paediatric and 1 adult B-ALL from different platforms. Moreover, it not only worked in full dataset, but also in subset of unknown cytogenetics. Additionally, the model also indicated differentiation trajectory in B cell development. Conclusion: We are able to develop a 9-gene score to fast calculate the risk of patient. The score is agnostic to platform, patient age, unknown cytogenetics.

Dr. Mahima Kapoor
Neuroscience

Title: *Clinical Challenges of Managing Inflammatory Neuropathies*

My PhD investigates a range of clinical challenges faced when managing inflammatory neuropathies. I initially investigated the incidence of thromboembolic events (TEE), over a period of 30 months in 112 neurology patients exposed to intravenous immunoglobulin (IVIg) and found that the incidence was greater than the NHS digital provided contemporaneous population-based TEE rates. Then, I compared the incidence between the initial 112 neuromuscular patients and 333 patients with other neurological diagnoses which reinforced that the incidence of arterial clots was significantly increased in patients exposed to IVIg, independent of other risk factors. Next, we aim to investigate the association between traditional and novel, neurology-specific risk factors, particularly exposure to IVIg, and the risk of cardiovascular disease in neurology outpatients. We are using the UK Biobank, whcih recruited 500,000 people aged between 40-69 years in 2006-2010 from across the country to quantify the attributable risk of IVIg independent of, and in interaction with, traditional risk factors. Combining risk factors will allow us to develop a risk prediction model which helps identify patients who would benefit from screening or surveillance of modifiable risk factors. Developing a neurology-specific risk score, may re-stratify neurology patients reducing missed opportunities for preventive interventions. If IVIg is identified as an independent risk factor, it may significantly impact our overall use of IVIg and long-term management of exposed patients.

Mr. Robert Cooper
MAPrc

Title: *Effects of frequency on enhancement and modulation of neural oscillations using brief transcranial alternating current stimulation (tACS).*

Theta frequency (4-8Hz) transcranial alternating current stimulation (tACS) was applied to assess the effects of brief periods of personalised theta stimulation on working memory performance and electrophysiological brain activity in a healthy population aged 18-45. The current study investigates the effects of a unique personalised approach to delivering transcranial electrical stimulation on brief time scales during cognitive tasks by targeting the fronto-parietal working memory network. The frequency of stimulation was individualised to each participant for each session. Individual theta frequency was determined by examining task relevant cortical locations, the frontal and parietal central electrodes. Electroencephalography (EEG) was performed while participants completed an initial N-back task. Individualised frequency was set based upon the frequency at which frontal and parietal electrodes were maximally correlated during correct memory maintenance to find a preferred communication frequency. Short periods of stimulation lasting 1, 5, or 20 seconds were randomly applied during performance of an N-back task or at rest, to attempt to enhance ongoing task related brain activity. Participants completed seven N-back tasks, T1 to T7, while either receiving active tACS, sham (placebo) stimulation, or received active tACS while at rest. Condition order was counterbalanced across participants using a within subjects design. Preliminary behaviour results (N = 8) suggest that the tACS condition had significantly higher accuracy during T5, with higher d-prime value at T5 and T6. Sham condition showed a faster reaction time at T7 only. All other time points were not significantly different.

Ms. Anna Harutyunyan
Neuroscience

Title: *GENE COEXPRESSION NETWORK ANALYSIS REVEALS COMMONLY DYSREGULATED INFLAMMATORY MODULES IN ALZHEIMER'S DISEASE AND TEMPORAL LOBE EPILEPSY*

Alzheimer's disease (AD) is a neurodegenerative disease affecting 50 million people worldwide. There is increased prevalence of epilepsy in patients with AD. Any common pathophysiology and cause-effect relationships between these conditions have been little-studied. With the accessibility of high throughput transcriptomics we now have the opportunity to define disease at a molecular level by constructing network graphs of differentially expressed/coexpressed genes involved in the dysfunctional pathways underlying diseases. The aim of this work was to investigate the mechanism of epileptogenesis in the setting of AD by identifying commonly dysregulated biological pathways and predict pharmacological targets for future treatment. Using a microarray dataset from post-mortem brain tissue of 64 AD patients and 64 non-demented controls, a tissue-specific gene coexpression network representing AD was constructed and divided into modules via WalkTrap algorithm. Pathway enrichment analysis revealed strong enrichment in inflammatory and synaptic pathways. A signature network graph of Temporal Lobe Epilepsy (TLE) was constructed from a previously published list of 442 epileptogenic genes. Significant enrichment in MAPK and innate immune system pathways was detected. Then, a network representing commonly dysregulated genes in AD and TLE was created by intersecting the gene networks of AD and TLE. The hub genes of highest degree betweenness in each module are implicated in GABAergic synapses and multiple inflammatory cascades. Both neuroinflammation and dysfunctional GABA receptors have been shown to generate seizures, and could explain the increased prevalence of epilepsy in AD patients. Future pharmacological studies targeting microglia to reduce seizure sensitivity in animal models are recommended.

Mr. Rishabh Sharma
Neuroscience

Title: *EFFECT OF AN ADDITIONAL IMMUNE CHALLENGE AFTER PAEDIATRIC TRAUMATIC BRAIN INJURY: MIMICKING HOSPITAL-ACQUIRED INFECTIONS*

Traumatic brain injury (TBI) is a major global health concern, with children being at highest risk of sustaining a brain injury. TBI patients are vulnerable to acquired infections that impede neurological recovery and worsen outcomes. Here, using a paediatric TBI mouse model, we hypothesised that a peripheral inflammatory challenge such as lipopolysaccharide (LPS), mimicking a hospital-acquired infection, would worsen TBI outcomes. Three-week-old mice received a moderate-severe controlled cortical impact or sham surgery, followed by a single LPS dose (1 mg/kg i.p.) or vehicle (0.9% saline) at 4 days. Mice were randomised to four groups; TBI+LPS, TBI+saline, sham+LPS and sham+saline (n=6-8/group). Post-injection sickness behaviours were evaluated, then blood, brains and spleen were collected at 5 or 8 days post-injury (=1 or 4 days post-LPS). LPS-treated mice exhibited a time-dependent reduction in locomotion and social investigation, and increased anxiety, alongside substantial body weight loss but increased spleen-to-body weight ratio, demonstrated transient sickness behaviours but persistent activation of adaptive immunity at 4 days post-TBI. Ongoing analysis of flow cytometry of brain, blood and spleen, as well as immunofluorescence staining of brain sections, will evaluate whether this transient immune challenge also contributes to an exacerbation of central and peripheral inflammatory responses to paediatric TBI.

Ms. Rosie Latimer
Melbourne Sexual Health Centre

Title: *Oh MG! The symptoms of Mycoplasma genitalium in women.*

Background: While the contribution of Mycoplasma genitalium (MG) to symptoms in men is well described, less is known about its clinical presentation in women. We undertook a study of 1200 symptomatic and asymptomatic women to determine the prevalence of MG and macrolide resistance and to determine its association with common genital symptoms in women to inform indications for testing. Methods: Women attending Melbourne Sexual Health Centre from 18/04/17 were tested for MG and macrolide resistance (ResistancePlusMG SpeeDx, Sydney), chlamydia and gonorrhoea (Aptima Combo 2, Hologic), trichomonasis (microscopy and culture) bacterial vaginosis (BV) and candida (microscopy). Women underwent examination and completed a questionnaire on symptoms. The prevalence of STIs, coinfection, and association with genital symptoms and signs was determined by univariate and multivariable analysis. Results: Of 1054 women enrolled to date (968 symptomatic and 86 asymptomatic), 62 (6%, 95%CI 5-7%) tested positive for MG, with macrolide-resistance detected in 54% (95%CI 41-67%). MG prevalence did not differ between symptomatic and asymptomatic women (6% vs 5%,p=0.614). Chlamydia and gonorrhoea were detected in 8% (95% CI 6-9%) and 1% (95%CI 1-2%), respectively. No specific genital symptoms or signs were significantly associated with MG, in contrast to chlamydia, which was associated with post-coital bleeding (OR 1.7, p=0.04) and cervicitis (OR 2.3, p=0.014). Conclusion: MG was as common as chlamydia in our clinic population but in contrast to chlamydia was not associated with any specific clinical features that would inform testing practices. Macrolide resistance was detected in 50% of cases.

Ms. Lakshanie Wickramasinghe
Immunology and Pathology

Title: *DEVELOPMENT OF A CLINICALLY RELEVANT MOUSE MODEL OF BRONCHOPULMONARY DYSPLASIA*

INTRODUCTION: Bronchopulmonary Dysplasia (BPD) is a severe lung disorder affecting premature infants requiring life-saving oxygen therapy. Currently, no cure exists and the treatments to prevent disease complications are inadequate, therefore better treatment strategies are urgently required. Due to the lack of gold-standard, clinically accurate animal model of BPD development, novel targets for therapeutic intervention remain unexplored. This study aims to develop a new supplemental oxygen mouse model of acute and chronic BPD, based on the key lung developmental stages affected in preterm infants with BPD. METHODS: Neonatal C57BL/6 mice pups were exposed to 75% oxygen for 5, 8 or 14 days from postnatal day PD1 to PD5,8 or 14 and /or kept in room-air conditions until PD40 to develop early and late-stage BPD. Mice lungs were assessed at PD14 and PD40 to examine the effect of differential supplemental oxygen schemes on the development of alveolar septal wall thickening and airspace enlargement. Mice housed solely in room-air served as disease free controls. Lung paraffin sections stained with H&E were used for morphometric analysis of structural changes. RESULTS: At PD14 and PD40, C57BL/6 mice exposed to oxygen from PD1 to PD14 had the greatest septal wall thickening and airspace enlargement, respectively, compared to the PD1 to PD5 and PD1 to PD8 supplemental oxygen protocols. The age-matched room air controls showed no changes to alveolar structure at PD14 or PD40. CONCLUSION: Supplemental oxygen exposures in the first 14 days of murine postnatal life can be used to accurately model key features of human BPD

Mr. Ryan Wick
Infectious Diseases

Title: *Metagenome assembly using long sequencing reads*

While DNA sequencing technologies have seen vast improvements over the past few decades, the sequencing data they generate is still fragmented and contains errors. An important first step in many analyses is therefore assembly: the reconstruction of the original genome, to the greatest extent possible, using imperfect sequencing data. Genome assembly can be challenging even for simple genomes, and the problem is particularly difficult when dealing with complex mixtures of genomes (a.k.a. metagenomes). In my research, I am exploring new algorithms for metagenomic assembly, which will lead to clearer insights into the genomics of human microbiomes and environmental microorganisms.

Dr. Robb Wesselingh
Neurosciences

Title: *Electroclinical Characteristics of Autoimmune Encephalitis as Outcome Biomarkers*

Introduction: Seizures are a common characteristic of Autoimmune encephalitis (AIE). There is a prevalence of 50-75% of seizures across the different serologic subtypes. The use of the electroclinical characteristics to assist in the diagnosis of AIE has been explored however use of specific electroencephalogram (EEG) changes has not been examined with regards to outcome prediction. Methods: Patients with AIE were recruited retrospectively across 4 hospitals in Victoria. Clinical Data was collected during admission and at final follow-up. EEGs of patients were reviewed using an objective proforma. Associations between EEG biomarkers and clinical outcomes were demonstrated using logistic regression modelling. Results: We recruited 88 patients with AIE and available EEGs. Presence of rhythmic delta, superimposed fast activity and an abnormal background were significantly more common in N-methyl-D-aspartame receptor (NMDAR) antibody associated AIE patients ($p<0.05$). ICU admission was associated with rhythmic delta epileptiform activity (OR 3.25, p=0.046), sharp elements in the EEG abnormality (OR 3.55, p=0.05), and an abnormal background rhythm (OR 3.56, p=0.03). Development of drug resistant epilepsy was associated with prolonged duration of abnormality on EEG (OR 11.99, p=0.013), and sharp elements in the EEG abnormality (OR 7.29, p=0.02). Conclusion: We have identified EEG biomarkers that differentiate NMDAR AIE from other subtypes, and likely represents an objective description of extreme delta brush which has previously been described in NMDAR AIE. We have also demonstrated biomarkers associated with important outcomes that can be used to help guide treatment and prognosis.

Mr. Wei Yeh
Neurosciences

Title: *Investigations of Vitamin D and Multiple Sclerosis*

Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease affecting the central nervous system and is an important cause of disability affecting young adults. Both genetic and environmental risk factors have been implicated in the development of MS. A significant observation is the presence of a latitudinal gradient of MS prevalence and incidence, with these increasing with distance away from the equator. The likely candidates to explain this observation is UVB exposure and vitamin D status. Epidemiological studies have also suggested a role of vitamin D in MS risk and disease activity. At the molecular level, vitamin D receptor (VDR) binding to the genome is enriched in regions of MS risk variants and a number of MS risk genes have been shown to have their expression modulated by vitamin D treatment. Vitamin D has immunomodulatory effects, overall promoting a regulatory tolerogenic phenotype. Few studies have explored the effects of vitamin D on immune cell function in the context of MS, and no studies have investigated alterations to the transcriptome by vitamin D supplementation in MS. This presentation will summarise the current knowns of the role vitamin D has in MS and will propose future directions for studies to further our understanding of this, particularly in the in vivo setting.

Poster presentation

Ms. Erica Plummer
Melbourne Sexual Health Centre

Title: *Gardnerella vaginalis clade distribution is associated with behavioural practices and Nugent Score in women who have sex with women*

Background: Gardnerella vaginalis is detected in women with and without bacterial vaginosis (BV). Identification of four G. vaginalis clades raised the possibility that pathogenic and commensal clades exist. We investigated the association of behavioural practices and Nugent Score with G. vaginalis clade distribution in women-who-have-sex-with-women. Methods: Longitudinal self-collected vaginal specimens were analysed using established G. vaginalis species-specific and four clade-typing PCR assays. Regression models assessed factors associated with G. vaginalis clade distribution. Results: Clades 1, 2 and 3, and multi-clade communities (>2 clades) were associated with Nugent-BV. Clade 1 (odds ratio[OR]:3.36; 95%CI:1.65,6.84) and multi-clade communities (relative-risk-ratio[RRR]:9.51; 95% CI:4.36,20.73) were also associated with non-optimal Lactobacillus deficient vaginal microbiota, suggesting increased pathogenicity. Clade 4 was neither associated with Nugent-BV nor non-optimal Lactobacillus deficient microbiota (OR:1.49; 95%CI:0.67,3.33), suggesting it may have reduced pathogenicity. Specific clades were associated with differing behavioural practices. Clade 1 was associated with increasing number of recent sexual partners and smoking, whereas clade 2 was associated with penile-vaginal sex and sharing of sex toys with female partners. Conclusions: Our results suggest that G. vaginalis clades have varying levels of pathogenicity, with acquisition occurring through sexual activity. These findings suggest that partner treatment may be an appropriate strategy to improve BV cure.

Ms. Sarah Griffith
Neuroscience

Title: *THE NEUROPSYCHOLOGY OF AUTOIMMUNE ENCEPHALITIDES*

Autoimmune encephalitides are a diverse yet rare group of neurological conditions presenting with acute or subacute confusion, behavioural change, cognitive and neuropsychological deficits and seizures. Due to rarity of these diseases and because of generally a psychiatric presentation, a number of cases of autoimmune encephalitis are missed or there is a significant delay in diagnosis. Individuals who develop autoimmune encephalitis have both subjective and objective cognitive deficits across the acute and chronic stage of illness. In the acute stage, global cognitive impairment is observed in patients, however the research is primarily derived from cognitive screeners, which are not sensitive or specific enough to determine a cognitive biomarker for subtypes of AE. Post-treatment, the cognitive profile is varied, and the literature is sparse – however, case studies often report significant verbal memory impairments and executive dysfunction. These cognitive impairments often result in difficulties reintegrating back into life, leading to reduced quality of life and significant psychological symptomology for patients. Given these conditions are only relatively newly discovered the neuropsychological manifestations, although a critical aspect of long term recovery, are not well described. The purpose of the studies is to, using both qualitative and quantitative methods, describe the distinctive neuropsychological phenotypes that accompany the various forms of auto-immune encephalitis in the acute and chronic stage, as well as assess the psychopathology and quality of life in these patients with the aim to inform diagnosis, prognosis and rehabilitation.

Ms. Georgia Symons
Neuroscience

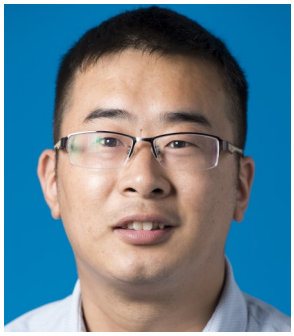
Title: *The neurological consequences of engaging in Australian collision sports*

Objective: Mild brain injuries, as a consequence of collision sport participation, have been linked to a range of neurological consequences. There is a need to identify biomarkers of neurological dysfunction and whether these abnormalities are mediated by a history of concussion (HOC) or biological sex. Methods: A case-control study was conducted investigating markers of cognition and neurological health in 101 Australian rules footballers (73 males, 28 females) (Australia's most participated collision sport), both with and without a self-reported HOC, in comparison to 50 control athletes (29 males, 21 females) with no history of neurotrauma or participation in collision sports. Ocular motor (OM) assessment was used to examine cognitive function. Telomere length, a potential biomarker of neurological health, was examined in saliva and blood. Results: Australian rules footballers exhibited reduced spatial accuracy to a remembered location on an OM memory guided task, as well as reduced salivary telomere length in comparison to controls. Both findings were independent of an HOC and sex. Salivary telomere length was associated with blood telomere length. Interestingly both saliva and blood telomere length correlated to reduced memory guided latency. Conclusion: Australian rules footballers, regardless of sex or an HOC, had demonstrable differences on OM function and telomere length in comparison to control athletes. These findings suggest that engagement in collision sports may be associated with neurological abnormalities, and that OM and telomere length measures may be sensitive biomarkers to monitor subclinical neurological injury in collision sport athletes

Ms. Nicola Sergienko
Baker Institute - Cardiac Hypertrophy Laboratory

Title: *B55alpha: A novel regulator of cardiac hypertrophy*

Introduction: Cardiac hypertrophy is an independent risk factor for heart failure. A key contributor to this maladaptation is activation of beta-adrenergic signalling in cardiomyocytes. B55alpha, a regulatory subunit of protein phosphatase 2A, modulates hypertrophic signalling downstream of beta-adrenergic receptors in vitro. To investigate the function of cardiac B55alpha in vivo, we generated mice with heterozygous (HET) or homozygous (HOM) deletion of the gene encoding B55alpha. Methods: Cardiac function, morphology, histology and molecular analyses were performed in i) a basal cohort (n=6-14/genotype, ~10-12 weeks of age, both sexes) and ii) a cohort subjected to 13 days of isoproterenol treatment administered via osmotic mini-pump (30mg/kg/day, n=5-6/group, male mice). Results: HOM mice were embryonically lethal. HET mice displayed a ~50% reduction in cardiac B55alpha expression (p=0.007) and showed no signs of pathology (normal systolic function, no fibrosis or induction of the cardiac stress markers Nppa and Nppb). Isoproterenol did not significantly increase heart weight/tibia length ratio of WT or HET mice, however HET mice displayed more pronounced changes in gene transcription. Specifically, expression of myosin heavy chain isoforms alpha and beta switched in favour of the beta-isoform in HET(p=0.004) but not WT (p=0.69) mice. This dysregulation is frequently observed in settings of cardiac hypertrophy and failure. Conclusion: Reduced B55alpha expression did not cause adverse remodelling in the murine heart in the absence of pathological stimuli. However, reduced B55alpha exacerbated hypertrophic gene transcription in response to sustained beta-adrenergic receptor stimulation, identifying B55alpha as a potential negative regulator of hypertrophic gene expression in vivo.



Mr Xianglong Xu
Melbourne Sexual Health Centre

Title*: How sequential sexual practices and saliva affect the transmission of Neisseria gonorrhoea: a mathematical model of multisite infection in men who have sex with men*

Background: Gonorrhoea is a common sexually transmitted bacterial infection both in Australia and globally. Understanding how gonorrhoea is transmitted between men is critical to developing interventions to control it. There is currently considerable controversy about how it is transmitted and particularly the role of that the oropharynx and saliva play. Gonorrhoea infection may affect multiple anatomical sites. However, only a recent study included multi-site infections in the model but could not perfectly simulate the observed joint prevalence values of site-specific gonococcal infection. We wanted to determine if sequential sexual practices and saliva during sex acts was included whether an improved simulation could be developed. Method: This study established a mathematical model of multi-site infection and self-infection employing a susceptible, infected and susceptible compartmental structure MSM. Monte Carlo simulations were performed in MATLAB R 2019a to solve differential equations. This study simulates the transmission of gonorrhoea from one anatomical site to another site in the same person through sequential sexual practices that involves saliva use with their partner. Result: The multi-site-infection model included the oral sex and anal sex in the same sexual episode or saliva use could produce the best estimates of the observed prevalence of gonorrhoea at each site (urethra, oropharynx and rectum). Conclusion: For a model to create the observed prevalence of gonorrhoea at each site, including multi-site infection, sequential sexual practices and saliva use needed to be included.

Ms. Alexandra Dimitropoulos
Diabetes

Title: *Impact of post-translational modification on the activity of glyoxalase-1: the relationship between structure and function.*

Modification of macromolecules such as proteins by excess sugar, known as glycation, ultimately leads to the formation and accumulation of Advanced Glycation End-products (AGEs). AGEs contribute to pathogenesis in a number of diseases including diabetic complications such as nephropathy, cancers and neurodegenerative diseases such as Alzheimers disease. An increase in glycolysis produces an excess of a key intermediate molecule, methylglyoxal (MG), which in turn reacts with proteins and modifies them to form AGEs. MG concentration is under the regulation of the glyoxalase pathway. When glyoxalase-1 (GLO1) activity is dysfunctional, MG accumulates which results in the increased formation of AGEs. GLO1 undergoes post-translational modifications (PTMs) and it has been shown that phosphorylation at T106 alters the activity of GLO1. It is currently unknown whether this PTM alters GLO1 activity due to an alteration of GLO1 structure. Studying whether PTM of GLO1 changes the structure of the protein and alters GLO1 function and activity will be the foundation for the discovery of GLO1-specific PTM inhibitors or generation of a constitutively active GLO1 protein. These would be promising tools in the context of alleviating the severity of diseases connected with the dysfunction of the glyoxalase pathway.

Ms. April Raftery
Immunology and Pathology

Title: *Immune and Inflammatory Mechanisms of Crohn's Disease*

Crohn's disease (CD) is a multifactorial, chronic, relapsing inflammatory bowel disease. Whilst the aetiology remains unknown, it is commonly hypothesised that dysbiosis of gut microbiota along with intestinal hyperpermeability and inappropriate inflammatory responses to commensal bacteria are potential mechanisms. Treatments are largely confined to general immunosuppressants, and although more targeted treatments are emerging, they are not effective in all patients. Therefore, an improved understanding of disease mechanisms could identify more effective treatment targets. In this project, the SHIP-1-deficient model of CD was used to examine the immune cell makeup and the impact of gut microbiota and intestinal barrier function on disease aetiology and progression. Additionally, the role of the gut-lung axis in driving disease was investigated. Histopathology studies showed that ileitis development in SHIP-1-/- mice was dependent on environment with mice housed in clean facilities producing the lowest disease penetrance. Mice without ileitis had normal ileal histology and no immune cell infiltration. SHIP-1-deficent mice with ileitis exhibited significant granulocyte infiltration as well as deficiency in γδ T cells and innate lymphoid cells which are important for intestinal barrier integrity. Severity of ileitis correlated to severity of lung disease; more inflammatory cell infiltration into the gut correlated to increased consolidation and emphysema in the lungs of the same mouse. Dysbiosis was evident in the ilea of SHIP-1-/- with ileitis characterised by a decrease in Sutterella (Proteobacteria phyla) and increase in Lactobacillus (Firmicutes phyla). This study has shown that environmental factors greatly influence disease onset and progression with housing and bacterial colonisation of the gut impacting on disease onset. Inappropriate innate and adaptive immune responses both contribute to pathogenesis of ileitis.

Mr. Muthukumar Mohan
Diabetes

Title: *THERAPEUTIC ACTIONS OF PRO-RESOLVING LIPOXIN A4 MIMETICS AGAINST ATHEROSCLEROSIS*

INTRODUCTION: Recent insights into the use of pro-resolving molecules, such as Lipoxin A4 (LXA4), has highlighted the novel therapeutic potential of Lipoxins against atherosclerosis, in mice with diabetes background. Here, we investigated the effectiveness of number of LXA4 mimetics in attenuating diabetes-associated atherosclerosis (DAA). AIM: The aim of this study was to investigate the therapeutic potential of LXA4 and two LXA4 mimetics against DAA in diabetic ApoE-/- mice. METHODS: ApoE-/- mice were rendered diabetic by five-daily intraperitoneal (IP) injections of streptozotocin (55mg/kg); control mice received citrate buffer. LXA4 and LXA4 mimetics were administered twice weekly for 10-weeks via IP injection in control and diabetic mice. At end-point, mice were culled and aortae collected and analysed for plaque deposition, gene expression, immunohistochemistry and histology. RESULTS: Preliminary results show that diabetic animals had increased blood glucose and serum glycated haemoglobin, as well as significantly elevated aortic plaque deposition (~5-fold) compared to control mice. Administration of LXA4 and mimetics significantly attenuated atherosclerotic plaque area (~70%). We also found that the mimetics significantly attenuated the TNFα induced inflammatory markers and cytokines (MCP1,IL1β,IL6,ICAM1,VCAM1,~50%) in primary endothelial cells and in primary aortic smooth muscle cells. CONCLUSION: To date, our findings reveal novel pro-resolving effects of LXA4 mimetics against inflammation induced-atherosclerosis, reversing inflammatory processes and plaque deposition. These results support our hypothesis that LXs can be used as a novel approach for the treatment of DAA.

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