

# 2018 CCS 11<sup>TH</sup> ANNUAL GRADUATE RESEARCH SYMPOSIUM

OF THE STUDENTS, BY THE STUDENTS, FOR THE STUDENTS



**Cover image: 2017 CCS Graduate Research Symposium**

Booklet compiled by Eliza Watson

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# Introduction

## 2018 Postgraduate Symposium at Alfred Centre, November 12, 2018

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 2018 Postgraduate symposium planning committee members are:



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*

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   | <b>\$400</b> |
| • Most outstanding poster presentation | <b>\$400</b> |
| • Second place oral presentation       | <b>\$200</b> |
| • Second place poster presentation     | <b>\$200</b> |
| • Third prize oral presentation        | <b>\$100</b> |
| • Third prize poster presentation      | <b>\$100</b> |
| • People's choice (oral presentation)  | <b>\$50</b>  |
| • Student raffle prize*                | <b>\$50</b>  |

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



*2017 Postgraduate symposium committee (L-R): Ms Michelle Flynn (Baker Institute), Ms Minhee Halemba (Vice-chair, ACBD), Mr Paul Gill (Gastroenterology), Mr Matthew Snelson (Diabetes), Ms Lakshanie Wickramasinghe (Immunology & Pathology), Mr Muthu Mohan (Diabetes), Mr Annas Al-Sharea (Chair, Baker Institute)*

# Program

**Monday 12<sup>th</sup> November, 2018**

10.00-10.10 am **Introduction & Welcome: Paul Gill, Chair student committee**

## **Session 1: Oral presentation**

**Chair: Angela Nguyen**

10.10-10.20 am Speaker: Mr Matthew Snelson

10.20-10.30 am Speaker: Ms Erica Plummer

10.30-10.40 am Speaker: Mr Jasper Cornish

10.40-10.50 pm Speaker: Ms Lakshanie Wickramasinghe

10.50-11.00 am Speaker: Ms Elizabeth Thomas

11.00-11.10 am Speaker: Ms Dijina Swaroop

11.10-11.20 am Speaker: Mr Daniel So

## **Session 2: Explain my graph Competition**

**Chair: Lakshanie Wickramasinghe**

### **Participants:**

- Prof Terence O'Brien (Neuroscience)
- Prof Peter Gibson (Gastroenterology)
- Prof Benjamin Marsland (Immunology)

**Judges:** Committee

**12.00-1.10 pm Lunch accompanying poster display (as listed under Session 3 below)**

## **Session 3: Poster presentations**

**Chair: Daniel So, Ee Yu**

(01) Presenter: Ms Anisha Ansari

(02) Presenter: Mr Martin Ezeani

(03) Presenter: Mr Michael Keating

(04) Presenter: Mr Rishabh Sharma

(05) Presenter: Ms Sarah Luu

(06) Presenter: Ms Paige Foletta

(07) Presenter: Ms Fiona McCutcheon

(08) Presenter: Dr Keith Potent

(09) Presenter: Mr Jack Jerome

(10) Presenter: Ms Magelage Perera

(11) Presenter: Ms Akshita Rana

(12) Presenter: Ms Michelle Wong

(13) Presenter: Ms Aleksandra Miljevic

(14) Presenter: Mr Habtamu Beyene

**Session 4: Oral presentation****Chair: Minhee Halemba**

1.10-1.20 pm	Speaker: Ms Amy Searle
1.20-1.30 pm	Speaker: Ms Angela Nguyen
1.30-1.40 pm	Speaker: Ms Larissa Ratten
1.40-1.50 pm	Speaker: Ms Amy Wilson
1.50-2.00 pm	Speaker: Ms Erica Kim
2.00-2.10 pm	Speaker: Dr Charithani Keragala
2.10-2.20 pm	Speaker: Ms Rosie Latimer

**Session 5: “No-Bell Prize” Competition for Supervisors**

2.20-2.40 pm	<b>Participants:</b> <ul style="list-style-type: none"><li>• Prof Nicola Harris (Immunology)</li><li>• Dr Chu Yao (Gastroenterology)</li><li>• A/Prof Mark Wright (Immunology)</li></ul>
	<b>Interviewing panel:</b> Daniel So, Paul Gill
	<b>Judge/Timekeeper:</b> Ee Yu
2.40-2.45 pm	<b>Representative from MPA</b>
2.45-3.00 pm	<b>Closing Remarks and Awarding of Prizes by Head of School, Central Clinical School, Prof Steve Jane</b>
3.00 pm	<b>Networking afternoon tea</b>

## Judges for presentations

### Judges for Oral presentations (session 1)



Chair:  
Ms Angela  
Nguyen



A/Prof Ross  
Dickins



Prof Kit Fairley



Prof David  
Tarlinton

### Judges for Oral presentations (session 2)



Chair:  
Ms Minhee  
Halembe



Prof Peter Meikle



A/Prof Joanne  
Fielding



Dr Jane Muir

### Judges for Poster presentations



Chair:  
Mr Daniel So



Chair:  
Ms Ee Fang Yu



Dr Steven  
Petratos



Prof Andrew  
Perkins



Prof Jenny  
Wilkinson-Berka

# Supervisor sessions

## 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.

## 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.



## Explain my graph 2017 winner

Professor Merlin Thomas (pictured right)



## Oral Presentation abstracts



**Mr Matthew Snelson**

Department of Diabetes

*Dietary resistant starch protects against diabetic nephropathy by inhibition of complement*

**Aim:** To investigate immune mechanisms by which resistant starch (RS) supplementation may be protective against diabetic nephropathy.

**Background:** Activation of complement occurs in diabetic nephropathy. C5a is a downstream complement component that activates the innate immune system contributing to inflammation. RS may be nephro-protective, however the effects of RS on complement activation and the innate immune system have not been explored.

**Methods:** Six week old non-diabetic mice (dbh), diabetic mice (dbdb) and dbdb mice on a regular chow diet supplemented with 25% RS (dbdbRS) were maintained for ten weeks. 24-hour urine was collected for albumin and C5a measurement by ELISA. Kidneys were digested and enriched for leukocytes using Percoll gradient. Cells were stained with CD45, CD11b, CD11c, Siglec F, Ly6C, CD86, C5aR antibodies and flow cytometry was performed.

**Results:** Diabetes was associated with an increase in albuminuria ( $28.0 \pm 6.5$  vs  $411.3 \pm 275.8 \mu\text{g}/24\text{h}$ ,  $P < 0.001$ , dbh vs dbdb), which was reduced in diabetic mice receiving RS supplementation ( $411.3 \pm 275.8$  vs  $125.6 \pm 37.3 \mu\text{g}/24\text{h}$ ,  $P < 0.01$ , dbdb vs dbdbRS). Urinary C5a excretion was increased by diabetes ( $92.6 \pm 17.6$  vs  $1324.0 \pm 429.7 \text{pg}/24\text{h}$ ,  $P < 0.001$ , dbh vs dbdb) and decreased by RS ( $1324.0 \pm 429.7$  vs  $577.7 \pm 123.1 \text{pg}/24\text{h}$ ,  $P < 0.05$ , dbdb vs dbdbRS). In diabetes there was an increase in CD86 MFI (a marker of activation) on infiltrating macrophages (Ly6C high), which was attenuated with RS ( $3.7 \pm 1.8$  vs  $1.5 \pm 1.0$  fold change to dbh,  $P < 0.05$ , dbdb vs dbdbRS). Furthermore, infiltrating macrophages were more likely to be positive for C5aR with diabetes ( $4.8 \pm 3.9$  vs  $54.0 \pm 27.8\%$ ,

$P < 0.001$ , dbh vs dbdb), which RS supplementation reduced ( $54.0 \pm 27.8$  vs  $11.7 \pm 4.2\%$ ,  $P < 0.01$ , dbdb vs dbdbRS).

**Conclusion:** These studies support the notion that RS is protective against renal disease via inhibition of complement.

## Oral Presentation Abstracts



**Ms Erica Plummer**

Melbourne Sexual Health Centre

*Sexual behaviours impact the vaginal microbiota of women who have sex with women*

We investigated the impact of sexual behaviors on the vaginal microbiota (VM) of women-who-have-sex-with-women (WSW) participating in a 2 year cohort study. Women self-collected high vaginal swabs and completed a behavioral questionnaire every 3 months for 24 months or until incident bacterial vaginosis (BV). We characterized the VM using 16S-rRNA gene sequencing of the V3V4 region. Community state types (CSTs) were identified using hierarchical clustering. Bacterial diversity was calculated using the Shannon diversity index and instability of the VM was assessed using change of CST and Bray-Curtis dissimilarity between consecutive longitudinal specimens. The impact of behaviours on diversity and instability of the VM was determined using multivariate regression models. Linear discriminant analysis effect size was used to identify bacteria associated with exposure to a new sexual partner. 360 specimens from 100 women were included in analyses. The VM clustered into five CSTs: three dominated by *Lactobacillus* species, one abundant in *Gardnerella vaginalis* and one of mixed bacteria. Exposure to a new sexual partner increased bacterial diversity (Adj coef=0.33, 95%CI:0.11,0.54) and instability of the VM, both in terms of change of CST (AOR=2.69, 95%CI:1.37,5.28) and increased Bray-Curtis dissimilarity (Adj coef=0.22, 95%CI:0.12,0.32). Sex with a new partner increased the abundance of bacteria often seen in BV including *G. vaginalis*, *Megasphaera* and *BVAB1* ( $p<0.05$ ). Conversely, no sex/sex in established ongoing relationships was associated with a favorable vaginal microbiota abundant in *L. crispatus*. Sex with a new partner markedly reshapes the VM of WSW by increasing the diversity and abundance of potentially pathogenic bacteria.



**Mr Jasper Cornish**

Burnet Institute

*The role of NFκB1 in follicular B Cell homeostasis and function*

Common variable immunodeficiency (CVID) is a disease characterised by enhanced susceptibility to recurrent infections, and frequent non-infectious complications, such as autoimmune disease and cancer. CVID aetiology depends on monogenic mutations, of which the most common in European populations is the haploinsufficiency of NFκB1. This gene encodes the longer p105 precursor protein that is cleaved to the shorter p50 form. Both p105 and p50 have undergone extensive characterisation, partly through use of the NFκB1-deficient mouse model (*Nfkb1*<sup>-/-</sup>). However, little is known regarding the impact of the heterozygous *Nfkb1* mutation in mice. We therefore examined young and ageing *Nfkb1*<sup>+/-</sup> mice, to ascertain the nature of *Nfkb1* haploinsufficiency. Young *Nfkb1*<sup>+/-</sup> mice displayed no overt signs of disease, but when challenged with lymphocytic choriomeningitis virus, displayed an impaired T cell-dependent B cell response. Additionally, *Nfkb1*<sup>+/-</sup> mice developed late-onset complications, including splenomegaly, multi-organ immune cell infiltration, and pulmonary inflammation. This pathology correlated with numerous immune defects, including the excessive production of CD4<sup>+</sup> T follicular helper cells and the enhanced generation of germinal centre B cells. In addition, we observed a marked expansion of an atypical CD21<sup>lo</sup> B cell population that expressed the key transcriptional regulator T-bet. Intriguingly, these late onset complications showed a marked gender bias toward female mice. Together, our findings lend support to the notion that *Nfkb1*<sup>+/-</sup> mice are a suitable model of human CVID, and extend our knowledge of this pathology.

## Oral Presentation Abstracts



**Miss Lakshanie Wickramasinghe**

Department of Immunology and Pathology

*Investigating the link between Bronchopulmonary Dysplasia (BPD) and Retinopathy of Prematurity (ROP) in preterm infants using animal models.*

Introduction: Bronchopulmonary dysplasia (BPD) and Retinopathy of Prematurity (ROP) are two debilitating disorders afflicting preterm infants. The overall incidence rate of BPD and ROP is about 50% and 98%, respectively, among infants with birth weights less than 1000g. Aim: To assess the potential link underlying the lung and eye disorders, a model of coincident BPD and ROP development was modelled using a gold standard, supplemental oxygen model of ROP. Methods: Neonatal C57Bl/6 mice were exposed to 75% oxygen (supplemental oxygen) for 5 days from postnatal day (PN) 7 until PN12. Mice were then returned back to room air (21% oxygen) until PN18, PN40 and PN80. Eye histopathology was assessed via lectin stained retinal wholemounts and Haematoxylin and Eosin (H&E) stained eye paraffin sections. Damage to alveolar structure was assessed via lung paraffin sections stained with H&E. Results: At the early time-points mild histopathology was evident in the lungs coincident with vascular degeneration in the retina in the oxygen groups compared to the room air controls. At the late time-points, the lesion progressed to severe airspace enlargement and simplification in the lungs, with concurrent thinning in choroid in the supplemental oxygen group. Conclusion: This model of coincident BPD and ROP provides an opportunity to evaluate the links between the two disorders which may involve inflammatory pathways. Translationally, this model could provide the opportunity to develop a treatment strategy targeting this pathway to simultaneously ameliorate these two debilitating disorders via a single therapy.



**Ms Elizabeth Thomas**

Monash Alfred Psychiatry Research Centre

*NRG1 genetic risk score predicts antisaccade and memory-guided saccade latency in schizophrenia*

Neuregulin-1 (NRG1), involved in neuronal development, migration, myelination and synaptic plasticity, has been identified as a promising candidate gene for schizophrenia risk. Several single nucleotide polymorphisms (SNPs) in the NRG1 gene have been associated with schizophrenia and cognitive deficits such as saccadic (eye movement) deficits. However, genetic liability for schizophrenia is multifactorial, with contributions of multiple risk variants. Therefore, analysis of genetic risk scores may better capture the genetic contribution to cognitive performance in schizophrenia. The aim was to investigate whether the genetic risk score for NRG1 predicts saccadic performance in patients and controls. One-hundred and sixty-six Caucasian participants (44 patients with schizophrenia/schizoaffective disorder and 122 healthy controls) completed the antisaccade and memory-guided saccade tasks, which engage spatial working memory and inhibition processes. Participants were also genotyped for five NRG1 SNPs; rs10503929, rs3924999, rs2466058, rs35753505 and rs6994992 and genetic risk scores were created. Antisaccade and memory-guided saccade latency and error rate were significantly different between patients and controls ( $p < 0.001$ ). In patients, the NRG1 risk score significantly correlated with antisaccade latency ( $p = 0.037$ ,  $r = 0.389$ ) and explained 15.1% of the total variance of the model. The NRG1 risk score also significantly correlated with memory-guided saccade latency ( $p = 0.018$ ,  $r = 0.435$ ) and explained 18.9% of the total variance of the model. There was no relationship between NRG1 risk score with antisaccade or memory-guided saccade performance in controls. These results identify NRG1 as a potential candidate gene for cognitive impairment in schizophrenia and support the use of aggregate genetic risk scores to investigate multifactorial disorders.

## Oral Presentation Abstracts



**Ms Dijina Swaroop**

Department of Medicine

*Bromodomain inhibition as a potential strategy to treat Head and Neck Squamous Cell Carcinoma*

Head and neck squamous cell carcinoma (HNSCC) is the sixth most prevalent cancer worldwide with 300,000 deaths and 550,000 new cases reported every year. Lack of targeted treatments have led to poor survival rate for this cancer with current five-year survival rate around 65%, which has changed only marginally in the past few decades. Our lab has previously elucidated a novel GRHL3/GSK3B/c-Myc signaling axis in HNSCC. I-BET 151 is small molecule inhibitor that perturbs c-Myc transcription by abrogating bromodomain recruitment to chromatin. We hypothesized that targeting c-Myc using I-BET-151 would be a potential approach in treating HNSCC. Efficacy of the drug was analyzed in diverse HNSCC experimental models including HNSCC cell lines and mice models. I-BET 151 perturbed proliferation and clonogenic capacity of the cell lines in-vitro. Reduced tumour growth and improved overall survival were observed in drug treated orthotopic xenograft mice models. In carcinogen treated models, treatment with IBET-151 significantly reduced tumour burden and increased tumour free survival in WT mice whereas the response to treatment was not significant in Grhl3 knockout mice. Thereby, these preclinical models have proven the promising therapeutic potential of I-BET 151 in HNSCC therapy. Extend of GRHL3 inhibition correlated with the drug effectiveness and this strategy could be applied in developing personalized therapies. Although targeting the GRHL3/GSK3B/c-Myc axis holds promise in HNSCC, pathway cross-talk and functional compensation from inhibiting single pathway members must be investigated prior to incorporating such therapeutic agents in to routine clinical care.



**Mr Daniel So**

Department of Gastroenterology

*Sugarcane fibre - Understanding of efficacy and value creation*

**Background:** The clinical value of specific fibres depends partly on their fermentation characteristics, traditionally assessed by extended incubations in vitro. This study aimed to utilise a new model that rapidly and dynamically assesses fermentation over 4 hours to compare fermentability of known and novel fibres.

**Methods:** Fibres (1g) were added to fresh faecal slurries from healthy participants (n=3) and fermented for 4 hours in chambers under anaerobic conditions. Substrates included known and the novel fibres, almond xylo-oligosaccharide (XOS-A) and sugarcane fibre (SCF). Endpoints included total gas production and changes in pH.

**Results:** Mean gas production over 4h was greatest for fructo-oligosaccharide (FOS; 76±26 ml/g) followed by corn-derived XOS (xylo-oligosaccharide; 66±3), inulin (47), XOS-A (26±8), partially hydrolysed guar gum (16) and SCF (3±1).

Differences were found for FOS vs SCF (p=0.01; uncorrected Fisher's LSD), XOS vs SCF (p=0.01) and FOS vs XOS-A (p=0.02). All fibres decreased faecal pH from baseline in proportion to gas production.

**Conclusion:** This model confirmed that fibre chain length influences fermentability, but also clearly showed that fermentability of XOS depends on its source and SCF is minimally fermentable. Extension of the results to the spectrum of individual gases may provide additional insights into the behaviour of fibres in vivo.

## Oral Presentation Abstracts



**Ms Amy Searle**

Baker Heart & Diabetes Institute

*Dual targeted theranostic delivery of micro-rna-126 arrests abdominal aortic aneurysm development*

Abdominal aortic aneurysm (AAA) is an often deadly disease without medical, non-invasive treatment options. The upregulation of vascular cell adhesion molecule-1 (VCAM-1) on aortic endothelium provides an early target epitope for a novel biotechnological theranostic approach.

AIM: To develop a novel theranostic approach toward AAA by utilizing a single-chain antibody targeted toward VCAM-1 and therapeutic microRNA-126 mimics coupled to echo-enhancing microbubbles (MBs).

METHOD AND RESULTS: MicroRNA-126 was used as a therapeutic agent, based on its capability to downregulate VCAM-1 expression in endothelial cells and thereby reduce leukocyte adhesion and exert anti-inflammatory effects. Ultrasound MBs were chosen as carriers allowing both molecular imaging as well as targeted therapy of AAA. MBs were coupled with a VCAM-1–targeted single-chain antibody (scFv<sub>VCAM-1</sub>) and a microRNA-126 mimic (M126) constituting theranostic MBs (TargMB-M126). In vitro experiments using VCAM-1–expressing SVEC4-10 cells provided initial evidence that TargMB-M126 downregulates VCAM-1 expression following an ultrasonic burst. In vivo proof of successful targeting of TargMB-M126 to VCAM-1–expressing endothelial cells was obtained in an LPS-induced mouse model of vascular inflammation. In vivo validation of TargMB-M126 using an Angiotensin II–induced AAA mouse model successfully demonstrated decreased vascular inflammation and significant prevention of AAA, which can be directly visualized in 3D ultrasound imaging.

CONCLUSION: Overall, we describe a unique dual targeted, biotechnological, ultrasound-based theranostic approach with the potential for early diagnosis and a long sought-after medical therapy of AAA.



**Ms Angela Nguyen**

Department of Immunology and Pathology

*Post-translational modification by N-glycosylation controls the binding of H2-Q10 to CD8aa*

Functioning as the central recognition element of antigen presentation, the major histocompatibility complex (MHC) is crucial for the elicitation of immune responses. Understanding the biology and interactions of these molecules is key in understanding immunity as a whole. Although not as well understood as their classical counterparts, non-classical MHC remain immunologically relevant due to their tissue restriction and highly specialised functions. Our group has recently characterised the non-classical MHC H2-Q10, which shows overexpression in the liver. Of particular interest is a novel interaction that occurs between H2-Q10 and the CD8aa homodimer expressed on gamma delta T cells. We have shown that this interaction is dependent on N-glycan structures present on CD8aa. We have also observed that the α3 domain of H2-Q10 is the point of contact for CD8aa binding and further determined key residues within the α3 domain that regulate this interaction. Our results have provided insight into the biochemical signature governing the novel interaction between H2-Q10 and CD8aa which provides a biochemical rationale for the exploration of CD8aa T cell biology.

## Oral Presentation Abstracts



**Miss Larissa Ratten**

Melbourne Sexual Health Centre

*Sexual Behaviours and Past Bacterial Vaginosis (BV) Contribute Significantly to BV Recurrence in Women Randomised to the Oral Contraceptive Pill*

**Introduction:** Bacterial Vaginosis (BV) is a state of vaginal dysbiosis and is the most common vaginal complaint in women. Epidemiological data suggests that combined (oestrogen-progesterone) oral contraceptive pill (COCP) favourably alters the vaginal microbiota and lowers BV recurrence risk. We conducted a randomised controlled trial of COCP-use after antibiotic treatment to examine its effect on BV recurrence. We present vaginal microbiota data from women enrolled in the trial. **Methods:** Participants provided monthly specimens for up to 6 months or until BV recurrence. 472 vaginal samples from 75 participants were selected for microbiota composition analysis by 16s rRNA V3V4 amplicon sequencing on the Illumina MiSeq platform. Longitudinal vaginal microbiota data were analysed for bacterial diversity and stability changes. Regression analyses were used to assess factors associated with increased diversity and stability, taking into account multiple specimens from each participant.

**Results:** Pre-treatment specimens had a *Gardnerella vaginalis* dominant or highly diverse vaginal microbiota. Post-antibiotic treatment, most women had a low diversity vaginal microbiota dominated by *Lactobacillus*. However, ongoing sex with the same RSP was associated with an increase in vaginal microbiota diversity (Shannon co-efficient=0.29, 95%CI: 0.02, 0.57,  $p=0.038$ ) and an increase in the abundance of *G. vaginalis* (AOR:3.58, 95%CI:1.16, 11.01,  $p=0.026$ ) after adjusting for BV history and COCP use. BV history was associated with decreased vaginal microbiota stability.

**Conclusion:** Women who had sex with the same RSP experienced an increase in bacterial diversity

and a higher abundance of key BV-associated bacteria including *G. vaginalis*. This supports mounting epidemiological evidence that reinfection with BV-associated bacteria drives post-treatment recurrence.



**Ms Amy Wilson**

Department of Immunology and Pathology

*Sitagliptin reduces tumour burden and restores anti-tumour immunity in an epithelial ovarian cancer mouse model*

Current methods used to treat epithelial ovarian cancer (EOC) often result in relapse and chemoresistance; therefore, novel therapies for EOC are urgently needed. Recent studies have suggested that sitagliptin, a dipeptidyl peptidase-4 (DPP4) inhibitor, can be used as a novel immunotherapeutic, however this has not been demonstrated in ovarian cancer. Additionally, no non-invasive preclinical models that allow us to study these therapeutic responses in vivo currently exist. We developed a model in which ID8 mouse EOC cells stably express a near-infrared protein (iRFP), then used this model to evaluate immune response and the anti-tumour effects of sitagliptin (50mg/kg/day) as a single therapy and in combination with paclitaxel (15mg/kg). Mice receiving combination therapy had reduced tumour burden, as indicated by fluorescence and macroscopic tumour observations. Sitagliptin increased the ratio of Teff/Tregs in the blood and peritoneum, and sitagliptin alone and combination therapy decreased myeloid-derived suppressor cells (MDSCs) in the peritoneal cavity. Paclitaxel alone depleted Teff cells, dendritic cells and Th1 cells, but combination with sitagliptin restored these immune populations. Taken together, these results suggest that administration of sitagliptin decreases tumour burden in an ID8 ovarian cancer model by shifting the balance toward anti-tumour immunity, and it may have therapeutic potential for EOC.

## Oral Presentation Abstracts



**Ms Erica Kim**

Department of Neuroscience

*Targeting EAE-induced demyelination and axonal pathology by transplanting haematopoietic stem cells that overexpress NgR(310)ecto-Fc fusion protein*

**Background:** Haematopoietic stem cell (HSC) transplantation is currently being trialed to treat multiple sclerosis (MS) as a means of modulating autoimmune-mediated inflammation and neurological disability. As MS is an immune-mediated neurodegenerative disorder, immunomodulation may not be effective for progressive neurodegeneration. Nogo receptor 1 (NgR1) is a high affinity receptor for myelin-associated inhibitory factors (MAIFs) that block for neurite outgrowth and may potentiate axonal degeneration in an animal model of progressive multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE). **Objectives:** HSCs can be utilised as carriers of the therapeutic protein for specific delivery into EAE lesions and can potentiate neurological recovery. **Methods:** As MS and EAE exhibit large numbers of inflammatory cell infiltrates within central nervous system (CNS) lesions, we utilized transplantable HSCs as a cellular delivery method of the NgR(310)ecto-Fc fusion protein.

**Results:** We have shown that we can deliver the specific NgR(310)ecto-Fc fusion protein through the transplantation of lentivirus (LV)-transduced HSCs that encode the NgR-Fc protein to sites of EAE pathology. We exclusively identified macrophages that were positive for the myc-tag (NgR-Fc-positive) occupying significant areas of inflammation and demyelination signifying the engulfment of NgR-Fc protein-MAIF complex by activated macrophages, which may increase the phagocytic activity of these populations and enhance repair. Importantly, n=3 animals transplanted with therapeutic NgR(310)ecto-Fc overexpressing HSCs, were rescued from symptoms associated with EAE.

**Conclusion:** Our results suggest that HSCs can be utilised as carriers of the therapeutic protein for specific

delivery into EAE lesions and can potentiate neurological recovery.



**Dr Charithani Keragala**

Australian Centre for Blood Diseases

*Fibrinolysis & innate immunity at play: complement inhibition reduces t-PA and plasminogen induced blood brain barrier (BBB) opening in vitro*

**Aim:** The relationship between fibrinolysis and innate immunity is evident in the increased BBB permeability induced by t-PA and Plg, which can trigger CNS infiltration by immune cells. Although Rho-Kinase 2 (ROCK-2) signalling plays an important role here, the pro-inflammatory properties of plasmin, including C3 and C5 convertase activity, are also likely to be involved. We aimed to characterise the effects of targeted complement inhibition on this phenomenon using in vitro BBB models.

**Methods:** An In vitro model of the BBB was used either using a monolayer of human brain endothelial cells (hBECs) or in a co-culture system with SVG human immortalised astrocytes. This was stimulated with t-PA+Plg in the presence or absence of complement fragment 5a receptor 1 inhibitor (PMX205). BBB permeability was assessed 4hr post-stimulation by evaluating fluorescent tracer passage from luminal to abluminal chambers. Permeability changes were calculated relative to a control unstimulated model. **Results:** PMX205 blocked permeability increases in stimulated hBECs monocultures, most notably at 100µM (p<0.01). PMX205 effect was comparable to KD025, which served as a positive inhibition control (p<0.01). Greater BBB protection by PMX205 was observed in the co-culture system, suggesting a central role of astrocytes in BBB sensitivity to complement. **Conclusion:** tPA and plasmin mediated BBB permeability is partly driven by C5a receptor activation. Inhibition of this, or with antifibrinolytics or ROCK-2 inhibitors may result in synergistic BBB protection. This has therapeutic implications in traumatic brain injury and stroke thrombolysis, where either endogenous or

## Oral Presentation Abstracts

administered tPA, can compromise the BBB causing secondary insults.



**Ms Rosie Latimer**

Melbourne Sexual Health Centre

*Clinical features of Mycoplasma genitalium associated pelvic inflammatory disease and response to moxifloxacin: a case series*

**Introduction:** There are limited data on clinical characteristics of Mycoplasma genitalium-associated pelvic inflammatory disease (MG-PID) which responds poorly to standard PID treatment regimens. While moxifloxacin is recommended in several treatment guidelines, published data to support its use in MG-PID are scant.

**Methods:** We conducted a retrospective study of women with PID in which MG was detected, as the sole pathogen at Melbourne Sexual Health Centre (MSHC), between 2006-2017. Clinical and laboratory characteristics of MG-PID were compared to cases of chlamydial PID (CT-PID) using multivariable analysis. The proportion of women with MG-PID achieving microbiological and clinical cure following moxifloxacin was determined.

**Results:** 92 patients with MG were treated for PID between 2006-2017, and were compared with 92 women with CT who were treated for PID. On multivariable analysis when compared to CT-PID, MG-PID was associated with increased lower abdominal tenderness [Adjusted Odds Ratio (AOR)=2.29 (95%CI 1.14-4.60)], but a lesser vaginal polymorphonuclear (PMN) response [ $>1-4$ PMN, AOR=0.34 (0.13-0.89)]. Of the 99 women with MG-PID, 54 received moxifloxacin (duration 9-14 days) and 37 returned for a test of cure between 14-120 days; 10 received moxifloxacin only and 27 moxifloxacin following a median of 7 days of a standard PID regimen. Microbial and clinical cure following moxifloxacin was 95% (95%CI 82-99) and 89% (95% CI 75-97), respectively.

**Conclusion:** MG-PID did not differ significantly from

CT-PID but was associated with more cervical/adnexal lower abdominal tenderness and less of a PMN inflammatory response. Moxifloxacin achieved high microbiological cure (95%), despite the emergence of quinolone resistance in Australia.

## Poster Presentation abstracts



### (1) Miss Anisha Ansari

Department of Immunology and Pathology

#### *Characterisation of murine non-classical MHC molecule, H2-M2*

Class Ib or non-classical MHC molecules are monomorphic, but are predicted to have quite diverse functions, although most have not been characterised yet. Studies using mouse models are essential for pre-clinical work. The murine Class Ib family has expanded to include 3 families: Q, T and M. Mice have this expanded family of non-classical MHC molecules that may be compensating or competing against the classical MHCs. Therefore, this warrants further study of these molecules to ensure translational studies remain relevant. H2-M2 is the most telomeric of the non-classicals, next to H2-M3 on chromosome 17 in mice. The only other M family member studied is H2-M3, which presents N-formylated bacterial peptides to cytotoxic T cells to initiate immune responses during infections with extracellular bacteria, such as *Listeria Monocytogenes*. Little is known about H2-M2, and existing literature has conflicting conclusions with regards to where H2-M2 is expressed. It will be interesting to determine the expression patterns of H2-M2 and going further to subcellular expression of H2-M2 in various immune cell populations in various mouse organs. Of great significance would be establishing the peptide dependence of H2-M2, the peptides it may present, and the cell types M2 may be interacting with. In terms of evolution, H2-M2 has diverged from the classical MHC molecules and is very different. As such, H2-M2 is predicted to perform roles other than antigen presentation to cytotoxic T cells. Together my research will aim to characterise this understudied non-classical molecule and determine functional consequences of a loss of H2-M2 in mice.



### (2) Mr Martin Ezeani

Baker Heart & Diabetes Institute

#### *The Roles of the p110 $\alpha$ Isoform of PI3K in Regulating Atrial size and its Therapeutic Implications in Atrial Fibrillation*

Atrial fibrillation (AF) is the most common form of arrhythmia in cardiology departments. Between 2014-2015, the Australian Commission on Safety and Quality in Healthcare estimated the number of hospitalisations for AF at 58,608, representing 430 hospitalisations per 100,000 people aged 35 years and above. This number is expected to double by 2034 due to the aging population, diabetes, obesity and heart failure. AF is characterised by fibrosis and an increase in atrial size. Individuals with minimal to severely dilated atria may be more likely to develop AF than those with normal atrial size. Left atrial diameter and volume stratification is an assessment for follow-up surveillance to detect AF in the clinics. Furthermore, a reduction in atrial size with surgical/treatment interventions is associated with a reduction in AF. In view of the common but challenging and complex arrhythmia, the Cardiac Hypertrophy laboratory at the Baker Heart and Diabetes Institute has generated heterozygote and homozygote dominant negative phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K) mice to assess the role of the p110 $\alpha$  isoform of PI3K in regulating atrial size and fibrosis. Hearts with normal PI3K activity are normal in size, and without fibrosis or AF. This study will assess the impact of decreasing PI3K (p110 $\alpha$ ) in the heart on atrial size, atrial fibrosis, and arrhythmia. Methods used will include echocardiography, electrocardiography, histology and molecular analysis. Normalising atrial size could represent an important strategy to prevent AF. Molecular based therapies which target the underlying mechanisms of AF, such as size and fibrosis, may be an alternative measure to current treatments of AF.

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### (3) Mr Michael Keating

Baker Heart & Diabetes Institute

*Psmc9 identified as a novel regulator of hepatic acylglycerol metabolism using an integrated systems-biology approach*

Disruptions in hepatic lipid homeostasis can promote the onset of conditions such as hepatosteatosis and insulin resistance. In order to interrogate hepatic lipid metabolism, we developed an integrated systems-biology discovery platform, consisting of 107 inbred mouse strains and performed proteomic and lipidomic analyses on the livers of these mice. We assessed protein:lipid associations in order to identify proteins/pathways not previously associated with hepatic lipid metabolism. This led to the identification of a protein known as 26S proteasome non-ATPase regulatory subunit 9 (PSMD9). PSMD9 highlights a previously underappreciated inter-play between proteostasis and acylglycerol metabolism. Moreover, the proteasomal associated protein was negatively associated with 65 lipid species in plasma and positively associated with 39 lipid species in the liver. Utilising the human hepatic cell line, Hep3B we sought to validate PSMD9 as a novel regulator of acylglycerol metabolism in vitro. PSMD9 overexpression resulted in a reduction in DGAT2 mRNA expression and an increase ABHD5 mRNA expression consistent with modulation of acylglycerol metabolism. Conversely, when PSMD9 was knocked down in cells DGAT2 expression increased and ABHD5 decreased. Acute over-expression of PSMD9 via an adenovirus (pAdV: PSMD9) in C57BL/6J and DBA/2J mice resulted in an accumulation of pathological acylglycerol and ceramide species in both the plasma and livers of these mice. Moreover, proteomic analysis of the livers of these mice revealed a significant enrichment of proteins associated with ER/lipid signalling and the proteasome. C57BL/6J mice injected with anti-sense oligonucleotides against PSMD9 resulted in

robust hepatic knockdown and modulation of hepatic and plasma lipid species.

These findings validate the discovery platform as a resource for identifying novel regulators of hepatic lipid metabolism. Moreover, they provide a novel link between proteostasis and acylglycerol accumulation, and validate PSMD9 as a driver of acylglycerol metabolism, which has implications for hepatic steatosis.



### (4) Mr Rishabh Sharma

Department of Neuroscience

*Peripheral immune challenge post-TBI exacerbate neuroinflammatory response and worsen outcomes.*

Traumatic brain injury (TBI) is a major global health concern, and results in a robust inflammatory response both peripherally and centrally. TBI patients are particularly vulnerable to acquired infections that in turn impede neurological recovery and worsen outcomes.

Here, using a mouse model of TBI, we tested the hypothesis that a peripheral inflammatory challenge such as lipopolysaccharide (LPS) associated with a hospital-acquired infection would worsen TBI outcomes by perpetuating the neuroinflammatory response. 10 week-old male C57BL/6 mice received a moderate-severe controlled cortical impact or sham surgery, followed by a single low LPS dose (0.33 mg/kg i.p.) or vehicle (0.9% saline) at 4 days. Mice were randomised to four groups; TBI+LPS, TBI+vehicle, sham+LPS and sham+vehicle (n=3/group). Acute post-injection sickness behaviours were evaluated, then brains were collected at 8 days post-injury for immunofluorescent detection of glial reactivity. Acute reduction in locomotion, increased anxiety, and substantial body weight loss in the TBI+LPS group demonstrated transient sickness behaviours in animals receiving a peripheral immune challenge at 4 days after a TBI. A robust increase in GFAP+

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astrocytes and Iba-1+ microglia/macrophages was observed in the ipsilateral cortex and hippocampus of TBI mice. However, whether peripheral LPS aggravates this response was inconclusive from this pilot study, likely due in part to the low dose of LPS used.

Next, we will profile inflammatory biomarkers in brain and peripheral blood by flow cytometry after a higher LPS dose, to better understand how a peripheral challenge after TBI influences the immune system and consequently functional outcomes.



### (5) Miss Sarah Luu

Australian Centre for Blood Diseases

#### *Residual splenic function after splenectomy*

**Aim:** To quantify rates of residual splenic function post-splenectomy using standard-of-care procedures.

**Methods:** Eligible participants were recruited from Spleen Australia clinical registry, were  $\geq 18$  years of age and had been splenectomised at least 1 year prior to their visit. Participants underwent screening for residual splenic function using a blood film and IgM B cell panel. Absence of Howell-Jolly bodies on blood film and normal marginal zone memory B cells indicated residual splenic function. Where screening was positive or unequivocal, screening tests were repeated and a  $^{99m}\text{Tc}$ -labelled heat-denatured red blood cell scan was performed to confirm functional splenic tissue with crude volumetric analysis. Based on screening and imaging results, participants were categorised into unlikely, limited or probable functional splenic tissue (FST).

**Results:** 75 splenectomised participants were recruited; 31 were male, average 57 years of age (range: 29 to 88), who had been splenectomised on average 19 years prior. Most common indications for splenectomy were trauma ( $n=23$ ) and haematological disease ( $n=21$ ). Screening tests revealed 10 had some degree of residual splenic function. One participant was excluded from further investigation due to previous imaging. Of the remaining nine, eight had some degree of functional splenic tissue on imaging (5 probable FST, 3 limited FST), with estimated volumes of ranging from 1.8 to 200 cc. 7 of the eight had been splenectomised for trauma. Overall, over 30% of trauma patients had some degree of residual splenic function.

**Conclusions:** Residual splenic function can be observed commonly in individuals splenectomised for trauma.

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### (6) Ms Paige Foletta

Department of Neuroscience

#### *Characterisation of Visual Snow: Modulation of Attentional Processes*

Visual snow (VS) is a persistent positive visual disturbance, described as the presence of tiny flickering particles across the entire visual field, akin to the 'snow' or 'static' seen on a poorly tuned analogue television. VS is a poorly understood phenomenon, though recently VS has proposed to be the defining feature of a VS syndrome with a unique underlying neuropathology. Recent studies have raised the suggestion that VS may arise from altered cortical excitability within the visual system, particularly the frontoparietal system. These systems are intimately connected to the attentional network. Ocular motor assessments of attention offer a sensitive method for interrogating the integrity of the neural systems implicated in VS. Preliminary data has observed shorter latencies and more errors to non-target stimuli in individuals with VS compared to controls. These findings are consistent with cortical hyperexcitability, either as a result of a failure in inhibition or an increase in facilitation. Further investigation is needed to fully characterise these deficits observed in VS, with a more comprehensive assessment of function likely to provide more insight into the pathophysiology underlying VS. Ultimately, ocular motor measures of attention may provide objective biomarkers of VS and an independent means of measuring treatment efficacy in a phenomenon long overlooked by the medical community.



### (7) Ms Fiona McCutcheon

Australian Centre for Blood Diseases

#### *Evaluating tissue-type plasminogen activator (tPA) as a novel therapeutic for Alzheimer's Disease*

Alzheimer's Disease (AD) is a severe neurodegenerative disorder that affects 44 million people worldwide, resulting in a significant financial burden for the healthcare system. To date no cure is available for this debilitating disease. Plasmin, the effector protease of the plasminogen activation system, can degrade amyloid beta ( $A\beta$ ), the peptide underlying the pathology of AD. Tissue-type plasminogen activator (tPA) is the main endogenous activator of plasmin, and tPA levels have been inversely correlated with numbers of  $A\beta$  plaques in the brain, suggesting a role of the plasminogen activation system in AD. To more closely evaluate the role of plasmin in AD pathology/onset, we aim to generate transgenic mice in an AD background that are overexpressing tPA in the brain and evaluate functional outcome and  $A\beta$  plaque load. Another aspect to this project will be to use intranasal delivery of tPA directly to the brain, an approach that has been previously validated in mouse models of traumatic brain injury and stroke. We hypothesize that intranasal delivery of tPA or Tenecteplase, an altered form of tPA that has an extended half-life, into APP/PS1 mice that are predisposed to AD, will improve outcome. We will be using zymographs to assess the activity of tPA/Tenecteplase and distribution in the brain. We are also aiming to assess behavioural outcomes and plaque loads at later stages of AD progression. This study will provide insights into the roles that tPA and plasmin are playing in AD and may provide a novel therapeutic option to improve outcome.

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### (8) Dr Keith Potent

Australian Centre for Blood Diseases

*Single site, open-label, dose-escalating, Phase I/II clinical trial of a synthetic bacteriophage delivering genetic cargo to metastatic solid malignancies in end-stage patients*

Background: Cancer is a genetic disease. Most cancer deaths are due to metastasis, yet metastatic disease is difficult to treat due to tumour microenvironment, multiple intracellular signalling pathways genetic mutations, mosaic (heterogeneous) cloning, and treatment resistance. The cost of metastatic disease to the Australian economy will exceed \$8B p.a. by 2030. To reduce human and socioeconomic impact, an effective cancer therapy needs to be engineered to overcome numerous mechanisms and kill the cancer cells while being safe, tolerable, and non-toxic to the healthy cells. Genetically-modified bacteriophages (GMBs), MetaVec, has been protein and genetically-engineered to deliver genetic cargo to cancer cells. Australia's regulatory and clinical trial environment are conducive to performing this world first phase I clinical trial to determine safety and tolerability of MetaVec in patients with metastatic disease. Methodology: Specifically, Maximum Tolerated Dose (MTD), Dose Limiting Toxicity (DLT) and recommended Phase II dose (RP2D) will be identified for defined schedule and mode of administration. Severity, duration, and reversibility of side-effects and target organs will be characterised for toxicity with regards to dose and schedule relationships. Initial characterisation of pharmacokinetics including dose and time-dependencies. This trial will be undertaken in cancer patients without established therapeutic alternatives. As per protocol, 10-15 patients will be infused with MetaVec up to  $1.5 \times 10^{11}$  particles (within-patient dose-escalation) in 100mL of normal saline for 30 minutes three days per week for three weeks. Toxicity will be evaluated using assessment of symptoms, physical examination, ECG, blood and urine laboratory analyses and radiological assessment as appropriate. Toxicity will be graded according to the Common Terminology Criteria for Adverse Events.



### (9) Mr Jack Jerome

Department of Diabetes

*Interrogating the immune mechanisms that underpin vision loss in systemic hypertension and diabetes*

Introduction: Diabetic retinopathy (DR) is the leading cause of blindness within the working population. Current treatments such as anti-VEGF intravitreal injections are limited with high proportions of non-responders, risk of injurious adverse events, and more critically a restricted capacity to regress pathology due to therapies targeting end-stages of disease. Therefore, new therapies are required to better target the mechanisms propagating pathology. The renin-angiotensin-aldosterone system (RAAS) may provide such opportunity as diabetes and hypertension, known DR risk factors, are strongly correlated with RAAS overactivity. Hypothesis: Through overactivity of the RAAS, diabetes and hypertension influence a systemic pro-inflammatory environment while concomitantly reducing immunosuppressive Foxp3+ T regulatory cell (treg) numbers. Therapies targeted at boosting Treg numbers such as RAAS inhibition, low dose IL-2, and adoptive Treg transfer will alleviate DR. Methods: Studies will be performed in diabetic and hypertensive rodents with research outputs of flow cytometry (FACS), quantitative polymerase chain reaction (qPCR), ELISA, and Evans blue. FACS will enable us to investigate changes in systemic immune cell populations. Meanwhile we can investigate pathogenic marker expression in the retina using qPCR and ELISA to determine mRNA, and protein expression respectively. Lastly Evans blue will allow us to assess the integrity of the blood-retinal barrier (BRB), as we expect our therapies to ameliorate DR-induced BRB breakdown. Results: Current preliminary FACS data from our rodent models has demonstrated the potential for RAAS inhibition to increase treg numbers in lymph nodes, and the spleen of hypertensive rodents when compared to their untreated hypertensive counterparts.

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### (10) Ms Magelage Perera

Monash Alfred Psychiatry Research Centre

*Therapeutic use of transcranial Alternating Current Stimulation for Obsessive Compulsive Disorder*

Obsessive-compulsive disorder (OCD) is a psychosocially incapacitating condition that significantly declines the quality of life of those affected. Due to our limited understanding of the underlying pathophysiology of OCD, successful treatment remains elusive. It is therefore, crucial to explore novel treatment approaches for treatment resistant OCD patients. Non-invasive brain stimulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have shown promising results towards improving OCD symptoms. However, TMS has several undesirable side effects including the potential to induce seizures, whereas tDCS cannot target the desired electroencephalographic (EEG) band forms that are implicated in OCD. Transcranial alternating current stimulation (tACS) is a novel and safe method of delivering a weak electrical current through the brain. The main advantage of tACS over other methods is its ability to individualize the treatment by delivering the current at a specifically targeted frequency related to abnormal cerebral electrical activity of each patient. Numerous studies suggest the presence of cerebral electrical activity derangements in OCD patients via electroencephalographic (EEG) analysis. Error related negativity (ERN) and N200 are parameters measured via EEG while the participant performs certain cognitive tasks. Both are found to be altered in OCD patients when compared to healthy controls. This study aims to conduct a randomized controlled study to establish whether alpha or gamma tACS has a therapeutic benefit in achieving significant improvement in oscillatory abnormalities of ERN and N200 of OCD patients.



### (11) Ms Akshita Rana

Australian Centre for Blood Diseases

*Shear-sensitive, single-chain antibody targeted nanocapsules: a novel platform for smart targeted antiplatelet drug delivery in extracorporeal membrane oxygenation (ECMO) devices*

Myocardial infarction and stroke have been the principal causes of morbidity and mortality. Current antiplatelet therapy involving systemic targeting of antiplatelet drug, results in a limited amount of effective drug concentrations at thrombus formation sites. At the same time, the bleeding complications including fatal bleeds may increase substantially. Hence, an effective targeted delivery of antiplatelet drug with increased local concentrations at thrombus sites is required to overcome these limitations. Nanocapsules (NCs) offer enormous possibilities for targeted drug delivery, owing to their high drug payload capacity and the ability for surface functionalization. However, therapeutic NCs have not been well exploited for the prevention or treatment of thrombosis or vascular remodeling.

It has been recently shown that arterial thrombosis and vascular remodeling are greatly enhanced by biomechanical forces, especially pathologic shear stress. Vessel stenosis due to large thrombus formation increases local shear 1-2 orders of magnitude. Nevertheless, current antiplatelet therapy has not been modified to respond to local prothrombotic effects of pathological shear stress. Taking these limitations in account, this project aims to develop shear-sensitive, phosphatidylcholine (PC)-based nanocapsules loaded with high-dose antiplatelet drug, to achieve shear-triggered delivery to the thrombus site. Active targeting of these liposomes will be further enhanced via conjugation to conformation-specific anti-GPIIb/IIIa single-chain antibodies (scFvs), that bind specifically to a ligand-induced binding site (LIBS) on activated GPIIb/IIIa. These single-chain antibodies will be

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essential in delivering drugs to evolving or established blood clots, enabling enhanced and localized therapy with no or reduced risk of bleeding. The antibody conjugated nanocapsules will be tested in microfluidic blood perfusion assays and into in vivo models of thrombosis and tail bleeding.



### (12) Ms Michelle Wong

Burnet Institute

*Targeting HIV in monocytes and macrophages to achieve HIV cure*

The persistence of HIV in cellular reservoirs is the most significant barrier to HIV cure. The establishment, nature and potential for latency in HIV macrophage reservoir is poorly defined in this highly heterogeneous cellular compartment. To investigate HIV reservoirs formation, monocytes purified from healthy donors (n=6) were infected with HIV in vitro before or after polarisation under inflammatory (M1) or non-inflammatory (M2) environments. Viral entry and productive HIV infection was measured by qPCR for HIV DNA, analysis of viral p24 by flow cytometry and reverse transcriptase activity in culture media. A HIV latency model is under optimisation using an HIV GFP reporter virus, with productive infection (GFP+ cells) detected by microscopy and the latent reservoir via sorting and qPCR for HIV DNA analysis in latent and uninfected macrophages (GFP- cells).

Analysis of polarised MDMs (infected prior to polarisation) demonstrated that p24 production was restricted by 68 -73% and 30 -77% in M1 and M2 macrophages respectively, compared to the unpolarised MDM population. In macrophages polarised prior to infection, an 8 - 42% reduction in total HIV DNA copies was observed for M1 macrophages, with varied effects in M2 macrophages. In both polarised states, the percentage of p24+ cells was reduced compared to

the unpolarised state. M1 polarisation inhibition of HIV occurred prior to viral DNA production whereas M2 polarisation affected protein production and viral release, indicating alternative pathways were induced by polarisation. The cytokine environment influences HIV replication in human macrophages and represents a potential, reversible mechanism for controlling latency.



### (13) Ms Aleksandra Miljevic

Monash Alfred Psychiatry Research Centre

*Associations between individual differences, rTMS-induced brain changes and relapse in depression*

Repetitive Transcranial Magnetic Stimulation (rTMS) is a recently approved and growing treatment for major depression. rTMS works by altering "abnormal" brain activity in the brains of individuals with depression, its application produces antidepressant-like effects on mood and cognition. Using electroencephalography (EEG), past research has characterised changes in brain activity of individuals with depression, before and after a course of rTMS. However, little is known of the long-lasting changes that may follow rTMS. Further, minimal research has examined brain activity changes that may occur prior to, or at onset, of depressive relapse. Therefore, this project aims to investigate the long-lasting brain changes produced by rTMS for depression, and how these changes might relate to depressive relapse or recurrence.

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### (14) Mr Habtamu Beyene

Baker Heart & Diabetes Institute

*The plasma lipidome response to an oral glucose challenge in apparently healthy young adults identified distinct perturbations associated with HOMA-IR*

Introduction: Type 2 diabetes is commonly preceded by compromised insulin sensitivity. The oral glucose tolerance test (OGTT) is used to detect insulin resistance and impaired glucose metabolism in apparently healthy people. We hypothesized that lipid metabolism would be altered in response to oral glucose challenge, and the resultant changes in the plasma lipid species would be associated with insulin resistance.

Method: A total of 246 non-obese, young adults aged 25-34 years were recruited. Plasma (10 $\mu$ L) from time 0 min and 120 min of the OGTT were collected and lipids extracted with a single phase butanol: methanol method. Targeted lipidomic analysis was performed by liquid chromatography mass spectrometry on an Agilent 6490 triple quadrupole. In total, 665 lipid species were measured. Changes in lipid concentrations were evaluated using paired Students t-tests.

Multivariable linear regression was used to identify associations of baseline lipids with HOMA-IR, and of the change in plasma lipid species in response to the OGTT with HOMA-IR.

Results: At baseline, phosphatidylethanolamine (PE), diacylglycerol (DG) and triacylglycerol (TG) species showed strong positive associations with HOMA-IR. Relative to baseline, the concentration of acylcarnitine, lysophosphatidylethanolamine, lysophosphatidylinositol, DG and TG species were significantly decreased following the OGTT. Fold change in several acylcarnitine, PE, DG and TG species were associated with HOMA-IR.

Conclusion: Multiple lipid metabolic pathways were perturbed in response to an OGTT. A blunted perturbation in acylcarnitine, TG, DG and PE pathways were associated with higher quartiles

HOMA-IR. These results provide new insight into the relationship between insulin signalling and lipid metabolism.

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