Friday 4th November 2022
9:00 am – 5:00 pm

Griffith University
Gold Coast Campus G40 (Level 5) Theatre 1
Parklands Dr, Southport, Queensland, Australia

Information about Griffith ECR Cross-Institute Symposium and program booklet is available on:
www.gcisymp.org

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ACKNOWLEDGEMENTS

Griffith University acknowledges the Traditional Custodians of the land on which we are meeting and pays respect to the Elders, past and present, and extends that respect to all Aboriginal and Torres Strait Islander people.

The 3rd Griffith University Early Career Researcher Cross-Institute Symposium organizing committee would like to extend their thanks to the Griffith students and staff for their participation and willingness to showcase their work. To the judges for their attendance, fairness and careful analysis of the research presented throughout the day – thank you.

Finally, we would like to take a moment to acknowledge and extend our thanks to Griffith Sciences, Griffith Health, Menzies Health Institute Queensland, Griffith Institute for Drug Discovery, Institute for Glycomics, Queensland Micro Nanotechnology centre, and our sponsors AGRF, Nikon, John Morris Group, Rowe Scientific, Miltenyi Biotec, Sarstedt, Pathtech, LabGear and Eppendorf who have kindly provided financial support for this event. We would like to thank Griffith University for providing the venue.

We are extremely grateful for all the support received. Without your support, we would not be able to host the event and provide lunches, tea breaks, awards and post-event celebrations.

THANK YOU

THE ORGANISING COMMITTEE

- *Dr Andrew Rayfield (MHIQ/GRIDD): a.rayfield@griffith.edu.au*
- *Dr Belinda De Villiers (Glycomics): b.devilliers@griffith.edu.au*
- *Dr Miaomiao Liu (GRIDD/ESC): miaomiao.liu@griffith.edu.au*
- *Dr Xiang Liu (MHIQ): xiang.liu@griffith.edu.au*
- *Dr Greg Tram (Glycomics): g.tram@griffith.edu.au*
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- *Dr Chin Hong Ooi (QMNC): c.ooi@griffith.edu.au*

OUR EVENTS

01 Symposium

2018

Definition in English:
1. A conference or meeting to discuss a particular subject
2. A collection of essays or papers on a particular subject by a number of contributors
3. A drinking party or convivial discussion, especially held in Ancient Greece after a banquet

Origin:
Late 16th century (denoting a drinking party): via Latin from Greek 'sumposion'; from sumpotēs 'fellow drinker', from sun- 'together' and potēs 'drinker'

Source: Oxford Dictionaries

02 Technology

2021

Definition in English:
1. Scientific knowledge used in practical ways in industry, for example in designing new machines
2. Machines or equipment designed using technology

Origin:
Early 17th century from Greek tekhnologia' systematic treatment', from tekhnē 'art, craft' + -logia (sayings, logy combining form denoting field of study).

Source: Oxford Dictionaries

03 Impact

2022

Definition in English:
1. The action of one object coming forcibly into contact with another
2. A marked effect or influence

Source: Oxford Dictionaries

The Definition of Research Impact :
Research impact is the contribution that research makes to the economy, society, environment or culture, beyond the contribution to academic research.

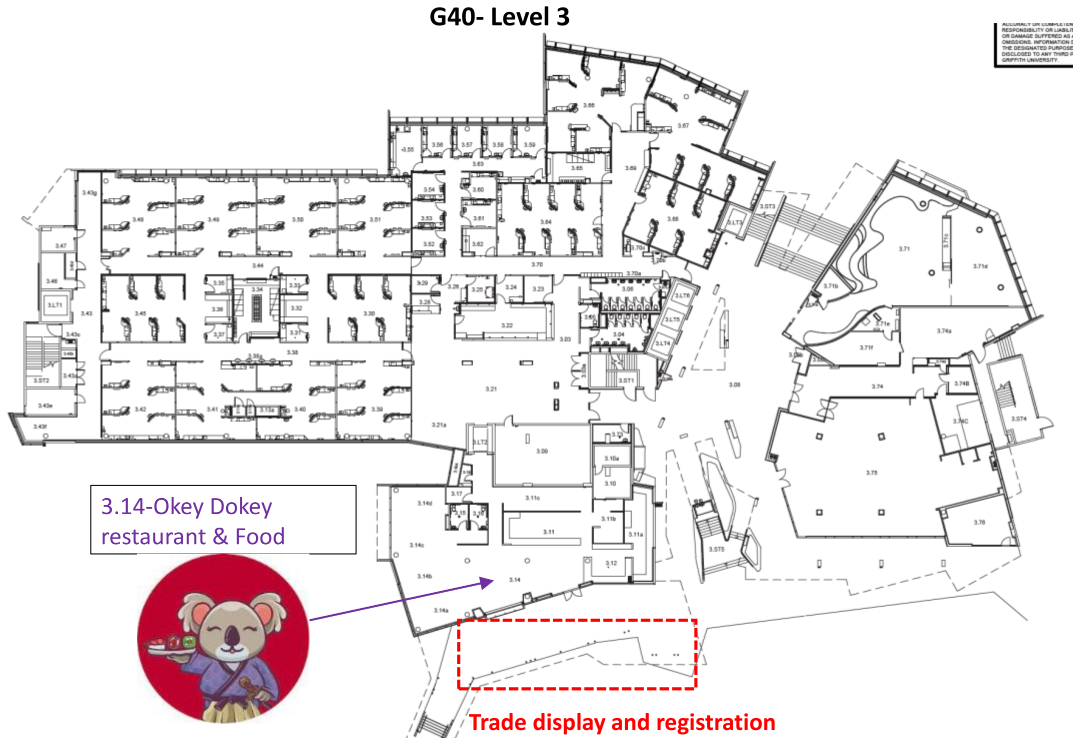
Source: Australian Research Council

Map

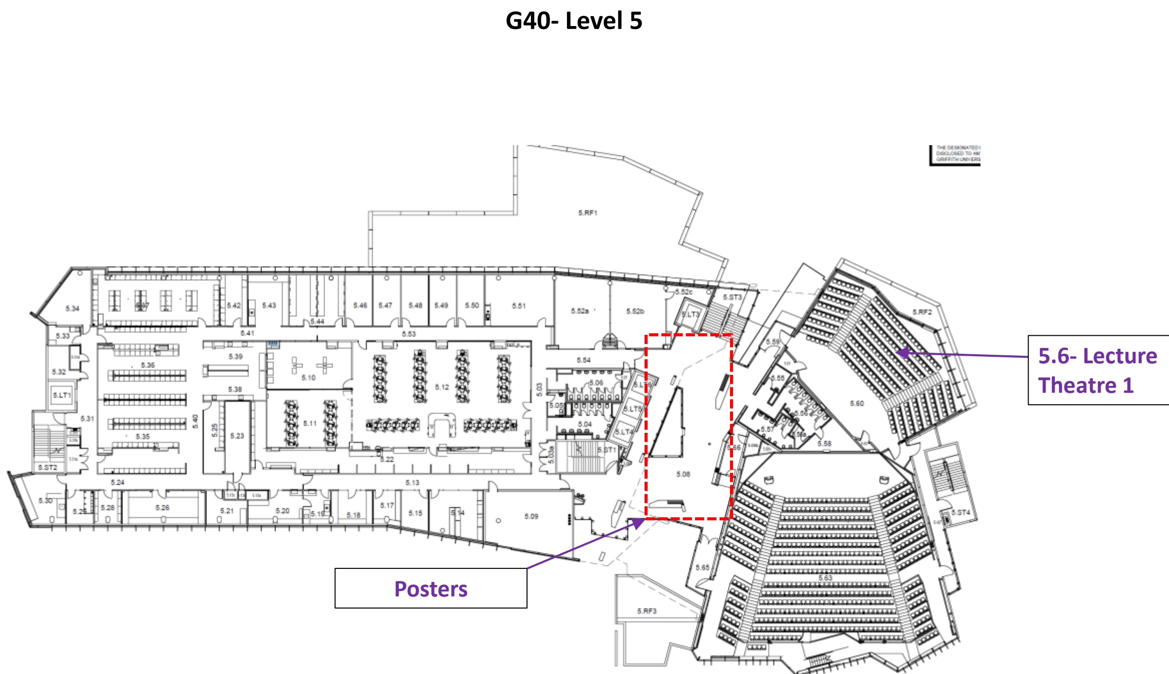
Symposium sessions and poster sessions: 9:00 am – 5:00 pm, G40 (Level 5) Theatre 1

Registration, trade display, morning/afternoon tea, lunch, social networking (5:30 pm – 8:30 pm): G40 (Level 3)

G40- Level 3



G40- Level 5

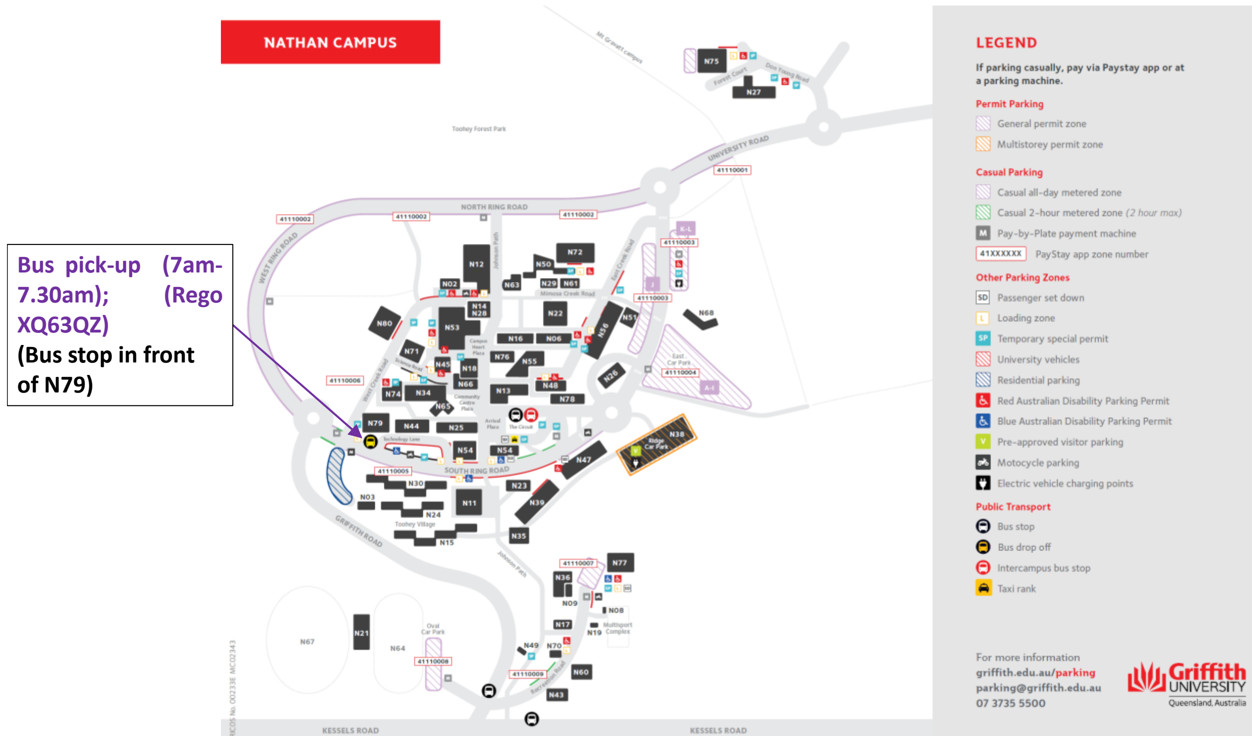


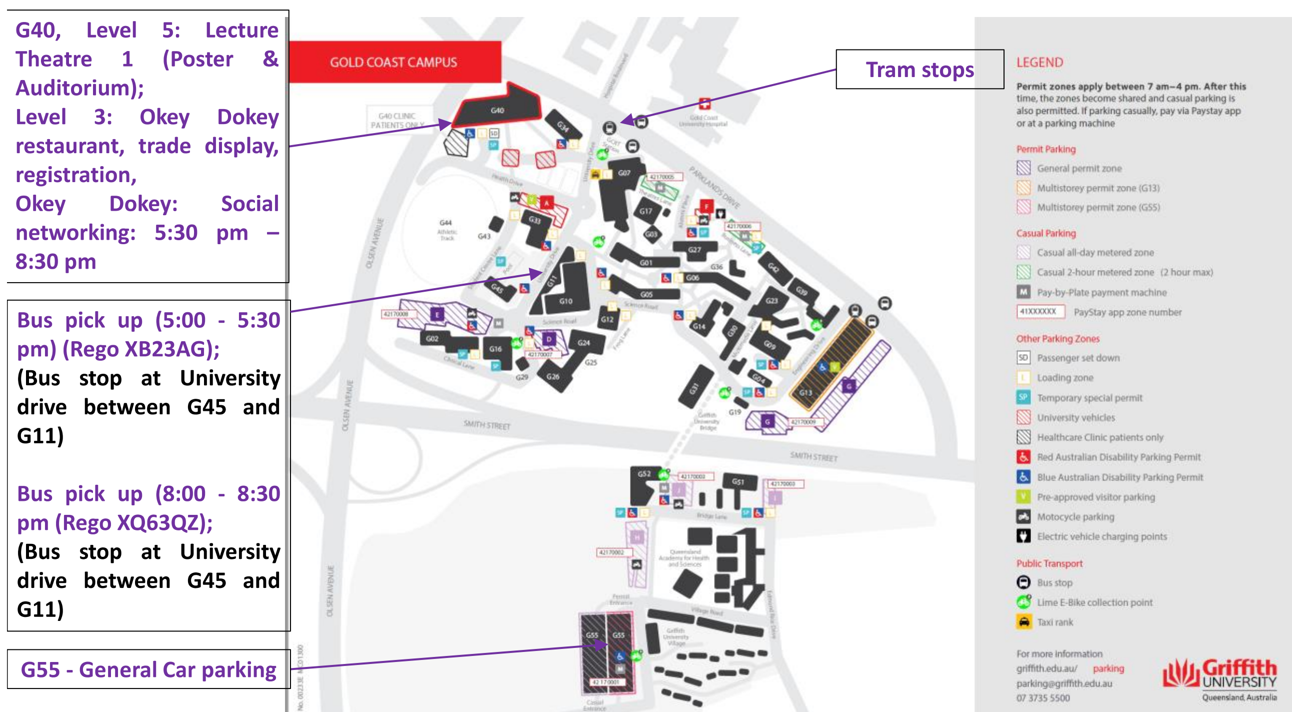
Bus

A **bus service** for transportation between the Gold Coast and Nathan campuses is available.

Pick-up is at Griffith University Nathan Campus, outside N79 at 07:30 am on 4th November 2022. The destination is the bus stop at University Drive (between G45 and G11), Gold Coast Campus.

Departure time from Gold Coast Campus back to the Nathan Campus will be 5:30 pm and 8:30 pm at the bus stop at University Drive (between G45 and G11).





Program

8:30 - 9:00	***Registration and morning tea***	
9:00 - 9:15	***Opening and Introduction***	
Session 1	***Chairs: Dr Andrew Rayfield / Dr Belinda de Villiers*** ***Session sponsored by Griffith Health***	
9:15 - 9:30	**O1:** Dr Jessica Poole Glycomics j.poole@griffith.edu.au	Utilizing the novel lectin abilities of CR3/Mac-1 to block *Neisseria gonorrhoeae*
9:30 - 9:45	**O2:** Dr Ali Delbaz MHIQ a.delbaz@griffith.edu.au	*Chlamydia pneumoniae* infects the brain via olfactory and trigeminal nerves and triggers Alzheimer's disease pathologies
9:45 - 10:00	**O3:** Dr Tamim Mosaiab Glycomics t.mosaiab@griffith.edu.au	Mechanisms of SARM1 activation and inhibition by small molecules
10:00 - 10:15	**O4:** Mr Rory Marriott QMNC rory.marriott@griffithuni.edu.au	Mathematical modeling of drug release from biodegradable polymers using compartments
10:15 - 10:30	**O5:** Ms Thilini Basnayake GRIDD bwmthilinij.basnayake@griffithuni.edu.au	Patient - derived tumouroids for personalized Head and Neck cancer modelling and drug screening
10:30 - 11:00	***Morning tea***	
Session 2	***Chairs: Dr Miaomiao Liu / Dr Gayathri Thillaiyampalam*** ***Session sponsored by MHIQ***	
11:00 - 11:45	**Plenary Lecture:** Dr Ali Zaid MHIQ a.zaid@griffith.edu.au	Viruses, Immunity and Inflammation: How Experimental Models Help Us Fight Diseases
11:45 - 12:00	**O6:** Mr Daniel Russell GRIDD daniel.russell2@griffithuni.edu.au	Epigenetic regulation of allele-specific expression in schizophrenia
12:00 - 12:15	**O7:** Mr Abolfazl Jangholi GRIDD abolfazl.jangholi@griffithuni.edu.au	Isolation of salivary and plasma exosomes for proteomic analyses in head and neck cancers
12:15 - 12:30	**O8:** Ms Xiaomin Huang GRIDD xiaomin.huang@griffithuni.edu.au	Circulating tumour DNA as a biomarker in head and neck squamous cell carcinoma
12:30 – 13:15	***Group photo and lunch***	
13:15 – 13:45	***Poster session 1*** ***Session sponsored by QMNC***	

<table>
<tr><td>*Session 3*</td><td colspan="2">*Chairs: Dr Ronak Reshamwala / Dr Xiang Liu*
Session sponsored by Glycomics</td></tr>
<tr><td>**13:45 – 14:00**</td><td>**O9:**
Dr Elke Kaemmerer
GRIDD
e.kaemmerer@griffith.edu.au</td><td>Multiplexed high-content imaging using cellular phenomics for drug discovery</td></tr>
<tr><td>**14:00 – 14:15**</td><td>**O10**:
Dr Sandra Duffy
GRIDD
sandra.duffy@griffith.edu.au</td><td>*Plasmodium falciparum* artemisinin resistance, an alternative view</td></tr>
<tr><td>**14:15 – 14:30**</td><td>**O11**:
Dr Jamila Iqbal
GRIDD
j.iqbal@griffith.edu.au</td><td>Impairment of LMO7 signalling pathway in schizophrenia patient-derived olfactory stem cells</td></tr>
<tr><td>**14:30 - 14:45**</td><td>**O12:**
Dr Shehzahdi Moonshi
QMNC
s.moonshi@griffith.edu.au</td><td>Folate decorated silver-Iron oxide nanorose enhances tumour targeting for synergistic photothermal therapy and dual MR & photoacoustic imaging</td></tr>
<tr><td>**14:45 – 15:00**</td><td>**O13**:
Mr Du Tuan Tran
QMNC
dutuan.tran@griffithuni.edu.au</td><td>Liquid marble – a novel high yield photo-microreactor platform</td></tr>
<tr><td>*15:00 – 15:30*</td><td colspan="2">*Afternoon tea and poster session 2*
Session sponsored by Griffith Science</td></tr>
<tr><td>*Session 4*</td><td colspan="2">*Chairs: Dr Jun Zhang / Dr Greg Tram*
Session sponsored by GRIDD</td></tr>
<tr><td>**15:30 - 15:45**</td><td>**O14**:
Dr Yuao Wu
QMNC
yuao.wu@griffith.edu.au</td><td>Metal oxide-chitosan compounds as theranostic modular nano-cocktails for ROS and inflammatory related diseases</td></tr>
<tr><td>**15:45 – 16:00**</td><td>**O15**:
Dr Pradip Singha
QMNC
p.singha@griffith.edu.au</td><td>Enhanced effective surface tension measurement using levitation-free oscillating liquid marbles</td></tr>
<tr><td>**16:00 – 16:15**</td><td>**O16:**
Dr Fahima Akther
QMNC
f.akther@griffith.edu.au</td><td>A novel microfluidic device for site-specific atherothrombosis formation and providing a patient-specific drug testing platform</td></tr>
<tr><td>**16:15 – 16:30**</td><td>**O17**:
Dr Karla Ximena Vazquez Prada
QMNC
k.prada@griffith.edu.au</td><td>Spiky silver nanoparticles for effective thrombolysis and multi-modal imaging of thrombosis</td></tr>
<tr><td>**16:30 – 16:45**</td><td>**Griffith Service Presentation:**
Dr Kyle Mathew Hatton-Jones
MHIQ
k.hatton-jones@griffith.edu.au</td><td>Central facility for genomics: A new GU initiative in spatial profiling</td></tr>
<tr><td>**16:45 – 17:00**</td><td colspan="2">***Closing, prize presentation and photos***</td></tr>
<tr><td>*17:30 – 20:00*</td><td colspan="2">*Social networking*</td></tr>
</table>

Poster presentations

P1- Inertial microfluidics: effective separation of CTCs from blood sample by embedding obstacle microstructure **Mr Haotian Cha** QMNC haotian.cha@griffithuni.edu.au
P2 - Prognostic utility of combining circulating tumour cells and cell-free DNA in non-small cell lung cancer **Dr Juliana Müller Bark** GRIDD j.mullerbark@griffith.edu.au
P3 – Contrasting metabolic effects of severe and moderate heat stress in Angus steers **Ms Alexandra Gloria** GRIDD a.gloria@uq.edu.au
P4 - An integrated analysis for discovering the impact of circular RNAs in schizophrenia derived olfactory neural stem cells **Mr Oak Hatzimanolis** GRIDD oak.hatzimanolis@griffithuni.edu.au
P5- Traversing chemical space with scaffold networks to identify structures relevant to Parkinson's Disease modulation **Ms Matilda Houston** GRIDD m.houston@griffith.edu.au
P6 - Metabolomic analysis of Wolbachia-infected Aedes aegypti **Mr Luke Husdell** GRIDD l.husdell@uq.edu.au
P7 - Collision-induced affinity selection mass spectrometry for identification of ligands **Mr Tin Mak** GRIDD tin.mak@griffithuni.edu.au
P8 - Dynamic tissue engineering: activating cells for neural repair **Ms Amy McEwen** MHIQ amy.mcewen@griffithuni.edu.au
P9 - Identification and characterisation of olfactory mucosal cell population **Ms Francesca Oieni** MHIQ francesca.oieni@griffithuni.edu.au
P10 - Optimisation of growth factor testing on olfactory ensheathing cells **Mr Tobias Seeberger** MHIQ t.seeberger@griffith.edu.au

P11 - Human tyrosinase inhibitors from natural resources as potential cure for skin hyperpigmentation
Mr Maxxie Shi
GRIDD
maxxie.shi@griffithuni.edu.au

P12 - Investigation of pneumococcal strains from infant nasopharyngeal samples
Mr Valentin Slesarenko
Glycomics
v.slesarenko@griffith.edu.au

P13 – Discovery Biology: Image-based drug discovery for protozoan pathogens
Dr Melissa Sykes
GRIDD
m.sykes@griffith.edu.au

P14 – Characterizing the role of miR-34a-5p in natural killer cell activation against cancer cells
Dr Gayathri Thillaiyampalam
GRIDD
g.Thillaiyampalam@griffith.edu.au

P15 - Antimicrobial metabolites of Bacillus Probiotics
Mr Charlie Tran
GRIDD
charlie.tran@griffithuni.edu.au

P16- NMR-based metabolomics to decipher the metabolic consequences of alcohol catabolism in cerebrospinal fluid
Ms Sarah Walsh
GRIDD
sarah.walsh3@griffithuni.edu.au

P17 - Deciphering the role of Carbonic anhydrase III in promoting cancer patient survival
Mr Yezhou Yu
GRIDD
yezhou.yu@griffithuni.edu.au

P18 - Prognostic utility of circulating tumour cells from head and neck cancer patients
Dr Xi Zhang
GRIDD
xi.zhang@griffith.edu.au

AWARDS

Research Excellence:

Oral Presentations:

ECR 1st Prize $300

ECR 2nd Prize $200

Student Prize $200

Poster Presentations:

1st Prize $250

2nd Prize $150

Audience participation prize: $100

This award is for a member of the audience who asks the best question(s) and engages with the speakers. We want to encourage questions and engagement from all participants, as ultimately this is what makes an exciting and interesting symposium.

Don't be afraid to ask anything!

FOOD ALLERGEN STATEMENT

Please note that food provided at this symposium may contain traces of milk, eggs, fish, crustacean shellfish, tree nuts, peanuts, wheat and soybeans amongst other known allergens. Consumption is at your own risk and Griffith University cannot be held responsible for adverse reactions.

There will be vegetarian options, free of gluten, lactose, dairy, nuts, passion fruit, ham, mushroom, or seafood. There will also be Halal options available, please speak to the organizing team for advice.

ORAL PRESENTATIONS

Plenary Speaker Oral Presentation

Viruses, Immunity and Inflammation: How Experimental Models Help Us Fight Diseases

Dr Ali Zaid

Menzies Health Institute Queensland, Griffith University

Viral infections have shaped mammalian immune systems for millions of years, yet represent a significant disease burden for humans. In this talk, I will outline examples that show how experimental models of viral disease can help us identify new targets, while unveiling complex - and sometimes unknown - host immune response mechanisms. Therapeutic approaches to treating viral diseases come in many forms, but some of the most successful strategies target host immune responses in order to alleviate clinical symptoms. Often, this means that poorly understood biological mechanisms need to be characterised to identify the best targets. With a focus on mosquito-borne viruses, I will showcase some of our group's recent findings, and demonstrate the usefulness of multidisciplinary approaches in projects aimed at tackling pathological conditions.

O1: Utilizing the novel lectin abilities of CR3/Mac-1 to block Neisseria gonorrhoeae

Jessica Poole[1], Christopher J. Day[1], Thomas Haselhorst[1], Freda E.-C. Jen[1], Victor J. Torres[2], Jennifer L. Edwards[3], Michael P. Jennings[1]

[1] Institute for Glycomics, Griffith University, Gold Coast Campus, Qld 4222, Australia
[2] Department of Microbiology, New York University School of Medicine, New York, NY 10016, USA
[3] The Center for Microbial Pathogenesis, The Research Institute at Nationwide Children's Hospital and The Department of Pediatrics, The Ohio State University, Columbus, OH 43205, USA

The human pathogen *Neisseria gonorrhoeae* uses glycosylated pili to mediate adherence to the I-domain of complement receptor 3 (CR3, CD11b/CD18) expressed on primary human cervical epithelial (pex) cells. Surface plasmon resonance was used to characterize the interaction between the I-domain of CD11b and di- or monosaccharide gonococcal pilin. There was no interaction with the monosaccharide modified pilin and the disaccharide pilin was determined to have an interaction with recombinant I-domain of CD11b 349 nM and 907nM with full length CR3. The role of the terminal galactose in this interaction was further verified using commercial glycans. It was found that a terminal galactose with any linkage was sufficient for binding to the I-domain with affinities of the interaction with free glycans ranging from 117-320 nM. Using an overlapping peptide library of the I-domain, the area of galactose binding was identified with the peptide G2 able to recapitulate the galactose binding of the full length I-domain. The G2 peptide was then used to block *N. gonorrhoeae* in both CHO-CR3 and pex cell models. A drug screen with the I-domain identified two candidates that were shown to prevent and treat gonococcal infection in the pex cell model. The interaction between the CD11b I-domain and the gonococcal pilin is mediated by terminal galactose binding to a small region of the I-domain and this region is sufficient for inhibition of N. gonorrhoeae in human ex vivo models with further work on this interaction identifying repurposed drugs that could both block and treat gonococcal infection in the pex cell model.

O2: *Chlamydia pneumoniae* infects the brain via olfactory and trigeminal nerves and triggers Alzheimer's disease pathologies

Ali Delbaz[1], Anu Chacko[1], Heidi Walkden[1], Souptik Basu[1], Charles W Armitage[3], Tanja Eindorf[1], Logan K Trim[4], Edith Miller[1], James A St John[1,2], Kenneth W Beagley[4], Jenny A.K Ekberg[1,2]

[1]Menzies Health Institute Queensland, Griffith University, Queensland
[2]Griffith Institute for Drug Discovery, Griffith University, Queensland
[3]School of Immunology and Microbial Sciences, King's College London, United Kingdom
[4]Centre for Immunology and Infection Control, School of Biomedical Sciences, Queensland University of Technology, Queensland

Mechanical stimuli, including fluid shear stress, osmotic pressure gradient, and extracellular matrix stiffness, significantly affect cellular interactions with drugs in biological structures. This paper introduces an integrated concentration gradient generator (CGG) capable of providing cell monolayers with these stimuli and demonstrates its design, fabrication, and quantification procedures. The proposed multi-layer chip consists of a CGG integrated with a membrane-based cell culture chamber (MCCC) and two bubble trappers for removal of micro-bubbles. The CGG provides cultured cells in the MCCC with four different concentrations of desirable inlet drug/chemical reagents. The MCCC is able to impose adjustable shear stresses, as well as osmotic pressure gradients on cell monolayers. The stiffness of the extracellular matrix (ECM) is also accommodating by utilizing a proper membrane in the MCCC. A numerical simulation based on the finite element method (FEM) is employed to design and optimize the integrated device, and then, the chip's performance is quantified using the experimental data. Finally, the biocompatibility of the proposed device is investigated by dynamic culturing of human lung cancer cells (A549 cell line) on the chip.

O3: Mechanisms of SARM1 activation and inhibition by small molecules

Yun Shi[1], Jeffrey D. Nanson[2], Weixi Gu[2], Todd Bosanac[3], Tamim Mosaiab[1], Veronika Masic[1], Faith Rose[1], Stephanie Holt[1], Lauren Hartley-Tassell[1], Eduardo Vasquez[1], Bostjan Kobe[2], Robert O. Hughes[3], and Thomas Ve[1]*

[1]Institute for Glycomics, Griffith University, Southport, QLD 4222, Australia.
[2]School of Chemistry and Molecular Biosciences, Institute for Molecular Bioscience and Australian Infectious Diseases Research Centre, University of Queensland, QLD 4072, Australia.
[3]Disarm Therapeutics, a wholly-owned subsidiary of Eli Lilly & Co., Cambridge, MA, USA.

Pathological axon degeneration is an early and a central feature of several neurodegenerative diseases. Sterile alpha and Toll/interleukin-1 receptor motif-containing 1 (SARM 1) induces the enzymatic cleavage of the essential metabolite nicotinamide adenine dinucleotide (NAD+) into nicotinamide (NAM) and adenosine diphosphate ribose (ADPR), which subsequently triggers axon destruction.1,2 Loss of SARM1 and its NAD+ glycohydrolase activity (NADase) protects axons in many neurodegenerative disease conditions such as neuropathies, glaucoma, and traumatic brain injury. Therefore, SARM1 is a promising therapeutic target but the molecular basis for its activation, substrate recognition and inhibition need to be explored.
Using crystallography, cryo-EM, NMR and biochemical assays, we demonstrate that SARM1 is activated by an increase in the ratio of NMN (Nicotinamide mononucleotide) to NAD+ and show that both metabolites compete for binding to the autoinhibitory ARM domain of SARM1.2 We show that NMN binding disrupts ARM-TIR interactions in the full-length SARM1 octamer, enabling its TIR domains to self-associate and form a catalytic site capable of cleaving NAD+.3 We also demonstrate that a potent SARM1 inhibitor undergoes base exchange with NAD+ to produce the bona fide inhibitor 1AD, and we describe structures of SARM1 in complex with 1AD and NAD+ mimetics.3 These structural insights identify SARM1 as a metabolic sensor of the NMN/NAD+ ratio, define mechanisms of SARM1 activation and inhibition, providing rational avenues for the design of new therapeutics targeting SARM1.

References:

1. Horsefield, S., et al. (2019). NAD+ cleavage activity by animal and plant TIR domains in cell death pathways. Science 365, 793–799.
2. Figley, M.D., et al. (2021). SARM1 is a metabolic sensor activated by an increased NMN/NAD+ ratio to trigger axon degeneration. Neuron 109, 1118–1136.e11.
3. Shi, Y., et al. (2022). "Structural basis of SARM1 activation, substrate recognition, and inhibition by small molecules." Molecular Cell 82 (9), 1643-1659 e1610.

O4: Mathematical modeling of drug release from biodegradable polymers using compartments

Rory Marriott[1], Tatiana Spiridonova[2], Sergei Tverdokhlebov[2], Yuri Anissimov[1], Owen Jepps[1]

[1]School of Environment and Science, Griffith University, Gold Coast
[2]The Weinberg Research Center, National Research Tomsk Polytechnic University

Polymer nanotechnology can be used to create controlled drug delivery systems that prolong the therapeutic effect of a wide range of drugs, as well as decrease their toxicity and increase patient compliance. Polymer delivery system development can be greatly facilitated by mathematical models that predict drug release rates from new systems. However, mathematicians who develop these models should take care to make them accessible to a wide range of clinical professionals and experimentalists, who may not have extensive mathematical education. Our group has developed a compartmental model to predict drug release from biodegradable polymers that is analogous to well-known pharmacokinetic compartmental models commonly used by pharmacists, making it more enticing for end-users. We have shown that the model predicts release rates at least as well as diffusion equation-based models for delivery devices displaying simultaneous diffusional and degradational drug release, while being less computationally demanding and more intuitive. It is straightforward to integrate the model into existing pharmacokinetic distribution models, to predict time-concentration curves inside plasma and other tissues after administration of a polymeric delivery system. We are currently continuing research into how the model can be adapted to describe more complex delivery scenarios, such as multiphase transport and the effects of unstirred boundary layers.

O5: Patient-derived tumouroids for personalized Head and Neck cancer modelling and drug screening

B W M Thilini J Basnayake[1], Paul Leo[2], Sudha Rao[3], Sarju Vasani[4,5], Lizbeth Kenny[5], Nikolas K Haass[6], Chamindie Punyadeera[1,7]

[1]GRIDD, Griffith University
[2]QUT/TRI
[3]QIMR
[4]Department of Otolaryngology, RBWH
[5]Cancer Care Services, RBWH
[6]UQ/ TRI
[7]MIHQ, Griffith University

Purpose: Human tumoroids have distinct features that make them one of the effective preclinical laboratory tools and Head and Neck Squamous Cell Carcinoma (HNSCC) Patient-derived tumouroids allow for the direct generation of laboratory drug screening models from patient tumour tissue, avoiding the requirement for prior modification or transformation.
Method: Twenty-three HNSCC patient samples were analysed to identify tumoroids. Immunofluorescence staining and drug sensitivity testing were used to characterise these tumouroids.
Results: HNSCC tumouroids were successfully established with a success rate of 63.33%. These tumouroids express epithelial and mesenchymal markers, allowing a better understanding of cellular behaviour, cell viability, and identity. The Cisplatin and Fluorouracil IC50 and their synergistic drug interactions were determined for HNSCC tumouroids using drug sensitivity assays using three different patient samples.
Conclusion: These tumoroids can predict in vivo drug susceptibility and may be effective tools for developing precision HNSCC treatments.

O6: Epigenetic regulation of allele-specific expression in schizophrenia

Daniel Russell, George Mellick, Alan Mackay-Sim, Alexandre S. Cristino

Griffith Institute for Drug Discovery, Griffith University, Nathan, QLD, Australia

In diploid organisms such as humans, there are two copies of each gene, or allele, one from each parent. Both alleles are expected to have similar activity, however, the level of expression between these alleles will not necessarily be identical.
Genomic imprinting is a process which results in one allele of a gene being silenced or having reduced expression in favour of the other based on the parental origin of the allele, which is thought to affect hundreds of genes. Many more genes also show this expression bias from one allele over the other, although this is due to gene regulation processes that have effects on each allele separately due to heterozygous genetic variants.
Genome wide association studies for schizophrenia have found most genes associated with this condition were in non-protein coding regions, this suggests that genetic variation to the regulation of genes were more associated with schizophrenia than variations to proteins themselves.
Using the whole genome sequencing and RNA sequencing data from human olfactory neurosphere-derived stem cells (ONS cells), bioinformatic tools were used to find 18 common genetic variants (single nucleotide polymorphisms, or SNPs) that displayed different levels of allele-specific expression between 8 schizophrenia patients and 9 controls. We also found little overlap between SNPs with allele-specific expression and public databases of imprinted genes.
A pilot study was completed using Oxford Nanopore Technology (ONT) to sequence the whole genome of 3 schizophrenia patients and 3 controls, measuring DNA methylation across their entire genomes. DNA methylation was analysed for 6 samples at one of the highest schizophrenia-associated loci (MIR137HG) and a well-known imprinted gene (MEG3).
All 8 schizophrenia patients and 9 controls in our cohort will have their DNA and RNA sequenced (using our ONT pipeline) to determine how modifications such as methylation on these nucleic acids differ between schizophrenia and controls, as well as their effects on allele-specific expression. Computational analysis of how heterozygous SNPs can influence transcription factor binding sites and micro-RNA binding sites and their effects on allele-specific expression will also be determined.

O7: Isolation of salivary and plasma exosomes for proteomic analyses in head and neck cancers

Abolfazl Jangholi[1], Juliana Müller Bark[1], Liz Kenny[2], Sarju Vasani[3], Sudha Rao[4], Riccardo Dolcetti[5], and Chamindie Punyadeera[1,6]

[1]The School of Environment and Science, Griffith Institute for Drug Discovery (GRIDD), Griffith University
[2]Royal Brisbane and Women's Hospital, Central Integrated Regional Cancer Service
[3]Department of Otolaryngology and the Department of Cancer Care Services, Royal Brisbane and Women's Hospital, Brisbane
[4]Gene Regulation and Translational Medicine Laboratory, QIMR Berghofer Medical Research Institute
[5]Sir Peter MacCallum Cancer Centre, The University of Melbourne
[6]Menzies Health Institute Queensland (MIHQ), Griffith University

Introduction/Background/Aim: Head and neck cancers (HNCs) are aggressive and clinically challenging tumours. Identifying sensitive and specific biomarkers is the best strategy for managing HNC patients and may improve prognostic and predictive accuracy and treatment outcomes. Exosomes have been suggested as potential biomarkers in cancer diagnosis and prognosis. However, the lack of standardized methods to isolate high-purity exosomes from complex biological fluids such as saliva and plasma is the bottleneck in the field. The main purpose of this study is to evaluate several exosome isolation protocols and determine which is the most appropriate for downstream analysis of protein abundance in exosomes derived from blood and saliva of HNC patients.
Methods: we have used ultracentrifugation (UC), ultracentrifugation plus filtration (UCF), size exclusion chromatography (SEC), and density gradient ultracentrifugation (DG) to isolate exosomes from saliva and plasma. The morphology, size, and concentration of exosomes were analysed using nanoparticle tracking analysis and transmission electron microscopy (TEM). Positive and negative exosomal markers were used to confirm the presence or absence of exosomes using western blot (WB). Quantitative proteomic analysis was applied to assess the protein profiles of exosomes.
Results: Among all methods, both DG and SEC methods provided higher exosome yields in saliva and plasma. However, exosomes isolated by DG (for saliva samples) and SEC (for plasma samples) showed higher purity than the other methods. TEM and WB analyses confirmed that all methods successfully isolated exosomes with an acceptable size range and morphology, but in the presence of some protein contaminations. The mass spectrometry analysis showed 382 proteins in UC, 306 in UCF, 311 in SEC and 328 in DG for saliva samples, and 204 proteins in UC, 204 in UCF, 316 in SEC, and 212 in DG for plasma samples.
Conclusion: Our preliminary data demonstrate that the exosome isolation method has an impact on the sizes, concentrations, purities, and proteomes. Further analysis is required to establish an exosome isolation method for saliva.

O8: Circulating tumour DNA as a biomarker in head and neck squamous cell carcinoma

Xiaomin Huang[1], Paul Leo[2], Sarju Vasani[3], Lizbeth Kenny AO[4], Pascal HG Duijf[2], Chamindie Punyadeera[1,5]

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[3]Department of Otolaryngology, RBWH
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Purpose: Except for viral-based head and neck squamous cell carcinoma (HNSCC) (HPV-related oropharyngeal carcinoma and EBV-related nasopharyngeal carcinoma), there are no clinically validated biomarkers for other types of HNSCC to early detect, prognosis and disease monitoring. Due to tumour heterogeneity, tissue biopsy sampling has a risk of missing clinically relevant clones. Circulating tumour DNA (ctDNA) are short nucleic acids derived from the solid tumour and circulate in the body fluid. We compared cfDNA isolation kits and quantified cfDNA concentrations (ng/ml of plasma) to HNSCC patients' clinical information. A gene panel for HNSCC patients is established and efficacy is tested by using whole exome sequencing (WES) data from patients' tumour DNA.

Methods: Three column-based cfDNA isolation kits were compared by using treatment-naïve cfDNA from six HNSCC patients. Using the optimal isolation kit, cfDNA was isolated using 60 treatment-naïve samples. Tumour DNA and the corresponding germline DNA from 10 HNSCC patients were done using WES. This mutational information was used to test the efficacy of the HNSCC gene panel.
Results: QIAamp Circulating Nucleic Acid Kit gave the highest cfDNA levels. HNSCC patients with tumour p16 negative had a higher concentration of cfDNA than those with p16 positive (7.48 vs. 4.27, $p<0.001$). Patients with N3 or Stage IV also showed higher cfDNA concentrations (8.18 and 7.51 respectively, $p>0.05$) compared to patients with other stages. HNSCC gene panel consisting of 55 cancer driver genes and more than 570 detection regions was established. Eight driver mutations involving four cancer driver genes (TP53, RIPK4, PIK3CA, EGFR) were discovered from the WES and all these driver mutations (100%) were included in our gene panel.

Conclusion: ctDNA demonstrates a promising prognostic biomarker in HNSCC. Our gene panel has high efficacy in testing driver mutations in HNSCC.

O9: Multiplexed high-content imaging using cellular phenomics for drug discovery

Elke Kaemmerer, Bilal Zulfiqar, Vicky M Avery

Discovery Biology, Griffith University

High content imaging, in combination with automated script analysis, is a powerful tool enabling extensive comparisons of numerous cellular features. When used for phenotypic screening in drug discovery, this approach distinguishes differences and similarities between cells, and can identify molecules directly impacting specific cell features.

Traditionally, phenotypic screening is based on the analysis of a small number of cell features and differences of these between samples, requiring specific staining of these features and customised analysis algorithms. To overcome the limitations associated with suitable dye and antibody combinations, as well as routine analysis based on intensity parameters alone, advanced phenotypic profiling using a generalised multiplexed approach can be used. Six or more specific dyes, or fluorophores, can be simultaneously used in conjunction with advanced feature extraction scripts to analyse thousands of morphological features associated with multiple organelles. Unbiased, automated algorithms, based on image segmentation to identify properties unique to an individual cell, results in feature measurements with a numerical value derived from the pixel information of each cell. This information, at the single-cell level, provides significant information about all cells within the sample. These feature measurements include standard cell morphology properties such as size, shape and intensity across a certain cell area and numeration of object counts, in addition to various organelle specific texture properties. This approach allows comparison of an extensive array of cellular features previously not detectable by traditional approaches, even without existing knowledge of affected cell features.

This innovative fully automated approach for high throughput screening, which is independent of the cellular deficit of diseased cells, provides a new platform for drug discovery across multiple disease indications. Cell profiling can be used to not only identify new lead molecules, but also improve understanding of cellular mechanisms involved in a disease and identify new targets.

O10: *Plasmodium falciparum* artemisinin resistance, an alternative view

Sandra Duffy, Vicky M Avery

Discover Biology

Over the past two decades significant advancements in the treatment and prevention of malaria have greatly reduced the number of infections and associated deaths. This has been largely attributed to a fast-acting, highly effective group of drugs known as artemisinins. However, in 2008 delays in parasite clearance time post artesunate monotherapy were observed in Western Cambodia, and this delay was subsequently linked to a mutation in the PF3D7_1343700 kelch propeller domain, commonly referred to as K13. Validated K13 mutations confer artemisinin resistance to very young ring-stage parasites in vitro and are heavily studied as the underlying cause of artemisinin resistance.

However, we recently identified that the genetic background associated with artemisinin tolerance, independent of K13 mutations, played a role in the in vitro ability of K13 mutant *Plasmodium falciparum* parasites to tolerate artemisinin derivatives. It is proposed that this genetic background, potentially acquired due to adaptation to chronic stress exposure, includes components of regulated cell death, which coincidentally impacts artemisinin tolerance.

In addition, we have recently published our findings on the impact of hyperoxia, a stimulator of oxidative stress, on *Plasmodium falciparum* artemisinin tolerance. Our data demonstrated that ring-stage parasite exposure to hyperoxia increased the artemisinin sensitivity of ring-stage parasites in the next parasite generation.

Collectively, these outcomes have led to a focus on the identification of a proposed regulated cell death mechanism in Plasmodium falciparum and its role in artemisinin tolerance. Biochemical, metabolic, and transcriptional studies have been initiated to evaluate this proposed mechanism.

We hypothesise that adaptation to chronic stress exposure may be an underlying key factor in drug tolerance, not only in Plasmodium but in other disease states such as cancers, diabetes, and neurological and cardiovascular diseases.

O11: Impairment of LMO7 signalling pathway in schizophrenia patient-derived olfactory stem cells

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Schizophrenia is a neurodevelopmental disorder that has been linked with the genes implicated in neuronal migration. Despite genetic contributions, the underlying molecular pathogenesis is poorly understood. Previously, ONS (olfactory neurosphere-derived) cells have shown subtle changes in migration speed and persistence on extracellular matrix substrates. Patient ONS cells show more directional persistence and smaller turn angles compared to the controls.

In this study, we investigated the molecular pathways underlying these processes. We constructed "protein-cell function interaction network" based on the differentially expressed proteins in patient ONS cells and controls to the cell phenotypes. We quantified the number of connections between proteins and functions and identified LMO7 as the most connected protein in the network. It was negatively correlated with the dynamic functions (Persistence time and Directionality ratio-half-life) and positively with the cytoskeleton measures. To validate these finding, the endogenous expression of LMO7 and other focal adhesion and cytoskeletal proteins in ONS cells was measured over time. Changes in cell migration was quantified using knockdown of LMO7 in multiple control and patient ONS cells.

Our results demonstrate that the endogenous expression of LMO7 links with the early events of cell adhesion. The migratory response of ONS cells to LMO7 knockdown recapitulates the Schizophrenia phenotype, consistent with the network analysis. This provides an insight into role of LMO7 in the neurodevelopmental mechanism and a potential therapeutic target for Schizophrenia.

O12: Folate decorated silver-Iron oxide nanorose enhances tumour targeting for synergistic photothermal therapy and dual MR & photoacoustic imaging

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Recently, nano-photothermal therapy (NPTT) based on nanoparticles (NPs) which converts near-infrared (NIR) light to generate heat to selectively kill cancer cells has attracted immense interest. This strategy demonstrated high efficacy and free of ionising radiation damage. We have designed a novel silver-iron oxide NPs (AgIONPs) which was successfully tuned for strong absorbance at NIR wavelengths to be effective in photothermal treatment strategy and dual imaging ability using MRI and photoacoustic imaging (PAI) in glioblastoma model. These nanoparticles are decorated with ligands targeting folate receptors that are highly expressed in various cancer types to enhance delivery and accumulation in tumour. Phantom studies of these nanoparticles demonstrated feasibility as a dual imaging contrast agent with decreasing T2 relaxivity and enhancement in photoacoustic (PA) signal intensity. Moreover, in vitro phantoms and in vivo MRI and PA imaging studies displayed preferential uptake of folate targeted NPs in U87MG (brain cancer) mice model indicating selective targeting efficiency of NPs. Notably, folic acid (FA) conjugation enhanced in vitro cytotoxicity of NPs (75.6% dead cells) and photothermal laser resulted in further significant synergistic killing of U87MG cells (100% dead cells). Importantly, intravenous injection of NPs in U87MG mice model resulted in significant tumour reduction and photothermal laser resulted in further substantial synergistic decrease in tumour size. Additionally, biosafety, and biochemical assessment performed in C57BL/6J mice displayed no significant difference between NP treatment and control groups. Overall, our FA-AgIONPs displayed excellent potential in the simultaneous application for a safe and successful targeted photothermal treatment and bimodal imaging of cancer model using MRI and multi-spectral optoacoustic tomography (MSOT).

O13: Liquid marble – a novel high yield photo-microreactor platform

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Transparent liquid marbles are becoming a research hotspot in recent time. The high transmission of light and large surface-area-to-volume ratio make transparent liquid marble the perfect candidate for microalgae culturing. In this study, we demonstrate for the first time the use of fume silica-coated liquid marble as the culturing platform for the growth of Chlorella vulgaris with a remarkable improvement in the culture yield compared to a conventional culture flask, with a significantly higher growth rate and a 30-time increase in the maximum cell density.

O14: Metal oxide-chitosan compounds as theranostic modular nano-cocktails for ROS and inflammatory related diseases

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Inflammation plays an essential role in the progression of many chronic diseases like hepatopathy, atherosclerosis and rheumatoid arthritis. Cytokines such as tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) play important roles in the regulation of the inflammation. In this study, modular two-in-one nano-cocktails were synthesised to provide treatment of inflammatory diseases and also enable tracking of their delivery to the disease sites. Chit-IOCO loaded with treatment module (cerium oxide nanoparticles) and imaging module (iron oxide nanoparticles) were synthesised by electrostatic self-assembly. Its MRI capability, anti-inflammatory and anti-fibrosis ability were investigated. Results demonstrated that Chit-IOCO significantly reduced the expression of ROS, TNF-α and COX-2 in the LPS-stimulated macrophages. Cytotoxicity studies showed that the nano-cocktails inhibited the proliferation of macrophages. Additionally, Chit-IOCO is a great MRI contrast agent in macrophages. It was possible to track the delivery of Chit-IOCO to the inflamed livers of CCl4-treated C57BL/6 mice, demonstrated by a shortened T2* relaxation time of the livers after injecting Chit-IOCO into mice. In vivo anti-inflammatory and blood tests demonstrated that Chit-IOCO reduced inflammation-related proteins (TNF-a, iNOS and Cox-2) and bilirubin in CCl4 treated C57BL/6. Histology images indicated that the nano-cocktails reduced fibrosis of CCl4-treated mouse liver and did not affect other organs of the mice. This is the first reported data on the anti-inflammation and anti-fibrosis efficacy of Chit-IOCO in C57BL/6 mouse liver inflammation model. Potentially, these nano-cocktails can be modified with antibodies or binding peptides, allowing these nanoparticles to target inflammatory biomarkers for the diagnosis of diseases. Moreover, conjugation of anti-inflammatory drugs could potentially enhance the therapeutic capability of these nano-cocktails. Overall, Chit-IOCO nano-cocktails have shown great potential in MR imaging/detecting and treating/therapeutic capabilities for inflammatory diseases and can be potentially applied for theranostics of atherosclerosis and rheumatoid arthritis in the future.

Reference:

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O15: Enhanced effective surface tension measurement using levitation-free oscillating liquid marbles

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A liquid marble is a non-wetting droplet encapsulated with micro-or nano-sized particles. Distinctive properties of a liquid marble such as low evaporation rate, low friction, and tunable porosity of the shell enable it to be a convenient tool for microfluidic applications. Recently, the fundamental research work on liquid marble focuses into understanding its stability, robustness, and effective surface tension. These key properties are inherently related to the structure and properties of the liquid marble shell. A liquid marble shell consists of encapsulating particles and the air pockets. The structure and the properties of the liquid marble shell depends on the properties of the encapsulating particles and the liquid marble preparation method. For an instance, effective surface tension values of liquid marbles prepared with encapsulating particles of different properties, are inconsistent. With the growing interest of liquid marbles in digital microfluidics, it is important to understand the factors for the inconsistent effective surface tension values and how such inconsistencies can be diminished. A major contributor to the inconsistent effective surface tension values could be the liquid marble preparation method. The most popular liquid marble preparation method is rolling a droplet on a hydrophobic powder bed. Scientists prefer rolling method as this is faster and more convenient. However, a manual preparation method does not consider the rolling parameters such as the duration of rolling or the rolling speed. The lack of control over the rolling parameters could result in the inconsistent effective surface tension values of a liquid marble. A systematic approach to prepare the liquid marbles, where the rolling parameters are kept constant should address the abovementioned issue. In this work, we are the first in i) determining the effective surface tension of a liquid marble utilizing its natural oscillation and ii) investigating the effect of the preparation methods on the effective surface tension values of a liquid marble.

We used a high non-uniform DC electric field to generate the dieletrophoresis force to oscillate the liquid marble at its natural frequency. Our method does not require contact angle measurement which is troublesome in case of a liquid marble. We compared the effective surface tension values determined by natural oscillation of the liquid marbles prepared by various preparation methods. We found that the effective surface tension values of the liquid marbles prepared manually are inconsistent. In contrast, a systematic preparation method using a vortex mixer at a constant rolling speed significantly enhances the consistencies of the effective surface tension values. Nevertheless, an excessive rolling speed causes interfacial jamming at the liquid marble shell and reduces the uniformity at the liquid marble shell. Such phenomenon at the liquid marble shell is responsible for the inconsistent effective surface tension values at higher rolling speed.

We believe our work could provide a new insight into the effective surface tension of a liquid marble, which could help digital microfluidics community. Further work could be dedicated to understanding the correlation between the effective surface tension, robustness, and stability at different liquid marble preparation methods.

O16: A novel microfluidic device for site-specific atherothrombosis formation and providing a patient-specific drug testing platform

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Atherothrombosis, an atherosclerotic plaque disruption condition with superimposed thrombosis, is the underlining cause of cardiovascular episodes. Understanding the pathophysiology of disease progression is the prerequisite for successfully treating this deadly condition. Patients at risk of atherothrombotic events are more likely to develop thrombus due to factors such as plasma glucose, lipid, and inflammatory cytokines. The primary prevention of atherosclerosis is using antiplatelet therapies. Nevertheless, the efficacy of antiplatelet therapies varies significantly between conditions with single and multi-diseases. It is essential to recognise and understand the advantages and risks associated with individual antiplatelet treatments as we move from population-based care to personalised care so that the appropriate therapy is given to the right patient at the right time. Herein, we present an in-vitro microfluidic-based model for real-time observation of the site-specific atherothrombosis formation and evaluating the risk of different factors in disease progression. The device consisted of two interconnected microchannels, viz main and supporting channels, where the former mimics the vessel geometry with different stenosis, and the latter introduces plaque components to the circulation simultaneously. A strong correlation was observed between vessel geometry and the thrombus formation phenomenon. Moreover, The model showed precise sensitivity toward high plasma glucose levels, elevated TNF-α, and increased plasma cholesterol levels in a dose-dependent manner. The model also effectively tests the aspirin efficacy in single and multi-disease patients for personalised dosing. Finally, the device effectively tested the targeted binding of the RGD (arginyl-glycyl-aspartic acid) labelled polymeric nanoparticles on the thrombus, which extended the use of our device to design targeted drug carriers.

O17: Spiky silver nanoparticles for effective thrombolysis and multi-modal imaging of thrombosis

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Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in Australia and the world, posing a tremendous social and economic burden to the healthcare system. Thrombosis and its complications are responsible for 30% of annual deaths. Limitations of current methods for diagnosing and treating thrombosis highlight the need for improvements. Agents that provide simultaneous diagnostic and therapeutic activities (theranostics) are paramount for an accurate diagnosis and rapid treatment, reducing rate of recurrence and death. We synthesised a novel theranostic spiky silver nanomaterial (AgIONPs) with strong absorbance in the near-infrared region by using iron oxide nanoparticle as seeding materials. The AgIONPs were biofunctionalized with different binding ligands for targeting thrombi and labelled with a fluorescence probe for optical imaging. In vitro binding assays showed a highly specific binding to human thrombus and activated platelets. In vitro fluorescence imaging and photoacoustic imaging (PAI) studies showed that AgIONPs can be used as a multimodal diagnostic agent for thrombosis. Laser-enhanced thrombolysis in vitro resulted in an increased effect of thrombolysis when exposed to 808 nm laser. In vivo imaging further corroborates the potential of AgIONPs as a multimodal contrast agent for PAI and fluorescence imaging, exhibiting in both significant enhancement of the image. Photothermal thrombolysis in vivo showed an increase in the temperature in mice treated with AgIONPs. Blood flow was restored in the targeted groups but not in the non-targeted groups. Thrombolysis from targeted group was significantly improved ($p<0.0001$) in comparison to the standard thrombolytic used in the clinic (tPA). Hemocompatibility assays on red blood cells, viability assays on CHO and endothelial cells, and histology analysis suggested no apparent toxic effects of AgIONPs. Altogether, our work suggests AgIONPs could be a potential theranostic agent for thrombosis.

Griffith Service Presentation:
Central facility for genomics: A new GU initiative in spatial profiling

Kyle Mathew Hatton-Jones

In 2021 GU established the Central Facility for Genomics to provide the University and its collaborators with the latest in genomics capability. With a NextSeq 2000, NanoString nCounter Digital Analyser, GeoMx and CosMx platforms and a 10X Genomics Chromium instrument, GU scientists can undertake spatial profiling, metagenomics (gut microbial profiling), single cell sequencing, gene expression, DNA sequencing and whole exome sequencing. This talk will focus on the NanoString GeoMx digital spatial profiling and CosMx Spatial Single Cell imaging platforms but will also provide an overview of the evolving field of spatial profiling and discuss some of the techniques involved, the advantages and disadvantages, and the study design considerations when undertaking spatial profiling

POSTER PRESENTATIONS

P1: Inertial microfluidics: effective separation of CTCs from blood sample by embedding obstacle microstructure

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Circulating tumour cells (CTCs) are cancer cells split away from the primary tumour. It is an important biomarker for liquid biopsy. However, they are very rare cells, typically 1-10 per mL of whole blood. Therefore, advanced technologies with high sensitivity and precision are highly needed!

Inertial Microfluidics is a size-based isolation technology based on the fluid's finite inertia with high flow speed. The benefits include high-throughput processing, simple channel geometry, and label-free and external field-free operations. This technology can provide highly promising results in the isolation of CTCs. However, the performance still needs to be improved to reach the level of commercial technologies. Therefore, innovative channel designs combining two or more geometries are promising to enhance the performance further.

This work explores embedding periodic concave and convex semi-circle obstacle microstructures in sinusoidal channels and investigates their influence on particle inertial focusing and separation. The concave obstacles could significantly enhance the Dean flow and tune the flow range for particle inertial focusing and separation. Based on this finding, we propose a cascaded device by connecting two sinusoidal channels consecutively for rare cell separation. The concave obstacles are embedded in the second channel to adapt its operational flow rates and enable the functional operation of both channels. The proposed device processed polystyrene beads and breast cancer cells (T47D) spiking in the blood. The results indicate an outstanding separation performance, with 3 to 4 orders of magnitude enhancement in purity for samples with a primary cancer cell ratio of 0.01% and 0.001%, respectively.

We believe our work of embedding microstructures as obstacles bring more flexibility to the design of inertial microfluidic devices, offering a feasible new way to combine two or more serial processing units for high-performance separation.

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P2: Prognostic utility of combining circulating tumour cells and cell-free DNA in non-small cell lung cancer

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Background: Lung cancer is one of the leading causes of cancer-associated mortality and accounts for 1.8 million deaths each year. Among lung cancer types, non-small cell lung cancer (NSCLC) is the most common. Despite recent advances, the prognosis of NSCLC patients remains poor, with a median overall survival of 12–18 months. Liquid biopsy-based biomarkers have emerged as potential candidates for predicting prognosis and response to therapy in NSCLC patients. This pilot study aimed to evaluate if combining circulating tumour cells and clusters (CTCs) and cell-free DNA (cfDNA) data can predict progression-free survival (PFS) in NSCLC patients.

Methods: CTC and cfDNA/ctDNA from advanced-stage NSCLC patients were measured at two time points, study entry (T0) and 3- months post-treatment (T1). CTCs were enriched using a spiral microfluidic chip and characterised by immunofluorescence. ctDNA was assessed using a commercially available mutation panel, UltraSEEK® Lung Panel. Kaplan-Meier plots were generated to investigate the contribution of the presence of CTC/CTC clusters and cfDNA for PFS. Cox proportional hazards analysis compared time to progression versus CTC/CTC cluster counts and cfDNA levels.

Results: Single CTCs were detected in 14 out of 25 patients, while CTC clusters were found in 8 out of the 25 patients at T0. At T1, CTCs were found in 7 out of 18 patients, and CTC clusters in 1 out of 18 patients. At T0, CTC presence and the combination of CTC cluster counts with cfDNA levels were associated with shorter PFS, p ¼ 0.0261, and p ¼ 0.0022, respectively.

Conclusions: Combining CTC cluster counts and cfDNA levels could improve PFS assessment in NSCLC patients. Our results encourage further research in larger cohorts to better understand the combined effect of CTC/cfDNA as a prognostic biomarker in advanced-stage NSCLC.

P3: Contrasting metabolic effects of severe and moderate heat stress in Angus steers

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Heat stress is an ongoing issue in the agriculture industry and animal production. In mammals, extreme heat stress causes catastrophic failures, including heat stroke, severe dehydration, and acute renal failure. Thus, efficient body thermoregulatory mechanisms are necessary to combat heat load. Black Angus steers (Bos taurus) are important for beef production, but they are more susceptible to heat stress due to their acclimation to temperate regions. It is important to understand the metabolic changes in Bos taurus due to heat stress to develop methods of offsetting its impact.

We subjected grain-fed Black Angus steers to two different heat load levels: severe (maximum Ta 40C, stepping down to 36 ℃ over seven days) and moderate (maximum Ta 35℃ over seven days). We found that steers drastically reduce their metabolic rate to decrease endogenous heat during a severe heat load. Metabolic changes include alterations in electrolyte balance and buffering, reduced gluconeogenesis, and using ketone bodies for fuel. This extreme survival mechanism contrasts with a moderate heat load, where steers experience slight metabolic perturbations, including negative energy balance and nutrient partitioning. When recovering from either level of heat stress, steers' metabolic states do not fully return to baseline days after the heat load event, suggesting they are in a homeorhetic state and that steers, regardless of treatment, require prolonged recovery periods from heat load events.

This study uses systems biology, specifically NMR-based metabolomics, and clinical biochemistry to provide a detailed biological analysis. Multivariate statistical analysis identified metabolites and clinical parameters that change significantly depending on the treatment level. Our expertise in combining the large, systems-wide method of 'omics technology with clinical data analysis provides impact by looking beyond conclusions previously published and make connections between animal physiology, endocrinology and metabolism like we have never done before.

P4: An integrated analysis for discovering the impact of circular RNAs in schizophrenia derived olfactory neural stem cells

Oak Hatzimanolis and Alex Cristino

Griffith Institute for Drug Discovery

Schizophrenia is a highly complex neurological illness whose aetiology and molecular mechanisms are not properly elucidated. Diagnostics and therapeutics for this neurological condition are limited to psychiatric evaluations and specific medications that have not changed drastically in the past half century. A promising area of research in molecular biology that is re-evaluating our understanding of schizophrenia is non-coding RNAs (ncRNAs). Approximately 85% of genetic variation in schizophrenia occurs in genomic regions responsible for ncRNAs. As a result, our research is focusing on a new class of novel ncRNA, termed circular RNA (circRNA), to explore untapped insights into novel molecular function and regulation. CircRNAs are highly stable due to their covalently closed ends, are abundant in most cell types and have higher reported expression in brain tissue comparatively to other types. They are also conserved evolutionary and present across all domains of life. Importantly, they have varying levels of biochemical functionality such as their ability to sequester (sponge) micro RNAS (miRNA) through binding sequences present on circRNAs. These miRNA are short ncRNAs (19-23 nucleotides long), with varying roles related to their binding with consensus sequences on mRNAs, inhibiting function and expression of said transcripts. This function as well as others has been studied in various types of cancer and conditions such as schizophrenia. So far, we have identified 9149 unique putative circRNA through a de-novo analysis from transcriptomic data for 18 schizophrenia and control patients using olfactory neural stem cells. From this we have found candidate circRNAs that are significantly differentially expressed in schizophrenia such as LM07, ZSWIM6, and PMS1. Comparative analysis between linear RNA and circRNA, as well as sequence motif analyses have been conducted. Through this, as well as future work in my doctoral program, such as oxford nanopore sequencing of circRNAs, we hope to discover new insights into the relationship circRNAs have with other ncRNAs and regulatory molecules and how this influences the cause and mechanisms of schizophrenia.

P5: Traversing chemical space with scaffold networks to identify structures relevant to Parkinson’s Disease modulation

Matilda Houston and Ronald J Quinn

Griffith Institute for Drug Discovery, Griffith University;

Introduction. Drug-development relevant chemical space (< 500 Da) is immense, consisting of around 1060 molecules. When exploring this vast chemical space through screening libraries, a significant factor in predicting success rates is the diversity of chemical scaffolds within the library. Scaffolds represent the core structure of molecules and are responsible for three-dimensional shape and orientation of substituents required for protein interactions, establishing the significance of scaffold selection in drug development. Scaffold networks allow us to traverse the full scaffold-space of molecular libraries by decomposing complex molecular scaffolds to generate scaffolds of different ring-sizes. Scaffold networks may be used to identify scaffolds associated with biological activity. In this nascent study (using a small dataset) a structure-activity approach to scaffold networks was undertaken with the aim to investigate the viability of this method in predicting scaffolds relevant to Parkinson’s disease modulation.

Methods. Results from a previous phenotypic screen of 90 natural products derived from traditional Chinese medicines on hONS cells were used for this study. Cytoscape was used to cluster the 90 molecules based on their biological effects on 28 phenotypic markers. Scaffold networks of the molecules were generated using the open-source program, ScaffoldGraph.

Results. Analysis and visualisation of scaffold networks for molecules with similar phenotypic profiles uncovered several scaffolds of interest which are potentially related to lysosomal activity in hONS cells.

Conclusions. This method could easily be scaled up to bigger databases, dependent on computational capacity. Larger, more diverse databases could allow the ability to predict relevant chemical space for PD research.

P6: Metabolomic analysis of Wolbachia-infected *Aedes aegypti*

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Wolbachia are obligate, intracellular bacterial symbionts of insects that have been proven to reduce transmission of viral diseases from insects to humans. Transfection of Wolbachia into the dengue mosquito, Aedes aegypti, has successfully reduced dengue transmission in 11 countries[1]. Wolbachia induces physiological changes in its hosts, but the mechanistic basis and the metabolic contributions to these host-symbiont interactions are unresolved. The Wolbachia genome lacks vital metabolism genes, suggesting the symbiont scavenges resources from its host. We employed 1H NMR-based metabolomics and targeted UPLC metabolite quantification to identify Wolbachia-induced metabolic changes. We investigated the infection of two strains, wMel and wMelPop, at two diet levels. The effects of diet overpower the metabolic changes attributed to wMel but did suggest that wMel participates in minor metabolic provisioning to Ae. aegypti. Conversely, wMelPop triggered immune system pathways including melanogenesis and reactive oxygen generation and management. Our research confirms that wMelPop is the more aggressive strain and triggers host immune responses, limiting wMelPop's ability to sustain infection in the field. In contrast, wMel is more benign to the host and thus more likely to form a stable inheritable infection. The strains wMel and wMelPop occupy distinct positions on the spectrum of mutualistic-parasitic symbiotic relationships that Wolbachia can exhibit.

1. World Mosquito Program, updated 2021, accessed February 2022, <https://www.worldmosquitoprogram.org>

P7: Collision-induced affinity selection mass spectrometry for identification of ligands

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Hyphenated mass spectrometry has been used to identify ligands binding to proteins. It involves mixing protein and compounds, separation of protein–ligand complexes from unbound compounds, dissociation of the protein–ligand complex, separation to remove protein, and injection of the supernatant into a mass spectrometer to observe the ligand. Here we report collision-induced affinity selection mass spectrometry (CIAS-MS), which allows separation and dissociation inside the instrument. The quadrupole was used to select the ligand–protein complex and allow unbound molecules to be exhausted to vacuum. Collision-induced dissociation (CID) dissociated the protein–ligand complex, and the ion guide and resonance frequency were used to selectively detect the ligand. A known SARS-CoV-2 Nsp9 ligand, oridonin, was successfully detected when it was mixed with Nsp9. We provide proof-of-concept data that the CIAS-MS method can be used to identify binding ligands for any purified protein.

P8: Dynamic tissue engineering: Activating cells for neural repair

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Introduction. Olfactory ensheathing cells (OECs) are the glia of the olfactory system which have a variety of roles in maintaining the health of the system. OECs are able to regenerate axons in the peripheral and central nervous system. This remarkable ability for axonal regeneration in the central nervous system has made them a leading candidate in cell-based therapies to treat spinal cord injury. Spinal cord injuries are a debilitating condition that currently has no treatment. OECs so far have been used in the treatment of spinal cord injury with varying success. It is believed this variation in success is due to a lack of a clear phenotype for OECs.
Methods. To study the phenotypes of OECs relating to their roles in vivo, transgenic mice were treated with methimazole, a drug extensively studied to induce a realistic injury model in the olfactory system. Injured mice and control mice were sacrificed at day 3 and day 10 and immunohistochemistry analysis was performed using Olympus FV3000 laser scanning confocal microscope. Results were attempted to be replicated in vitro using primary OECs cultured from transgenic mice and treated with different inflammatory conditions.
Results. Three clear morphologies were defined: O1 – resting OEC was the morphology relating to the control healthy condition; O2 – phagocytic OEC relating to the phagocytic role of OECs following immediate damage; and O3 – reparative OEC was seen after the system had begun repairing itself. OECs were also studied in vitro to attempt to induce the morphologies seen in vivo.
Conclusion. The study was successful in illustrating three distinct OEC morphologies in vivo. Further, optimisation of in vitro assays is needed to mimic the in vivo environment.

P9: Identification and characterisation of olfactory mucosal cell population

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Introduction. Spinal cord injury is a devastating condition with little scope of healing with available medical options. Cell transplantation with olfactory ensheathing cells (OECs) shows great promise in the preclinical studies, however, obtaining pure cells from mucosa remains a challenge. OECs in mucosa are accompanied by fibroblasts. It is also proposed that the best outcomes may be achieved with an ideal mixture of the two cell types rather than a single pure population. However, the two cell types share many key characteristics, making identification and characterisation of the cell population difficult. In this study, we identify characteristics of both cell types to better define the two populations and to establish robust pipelines for studying their interactions.
Methods. We optimised the workflow olfactory ensheathing cell (OEC) and mouse embryonic fibroblast (MEF) with cell-lines and used that to characterise the primary mouse mucosal OECs and fibroblasts. The assessed parameters are as follows: a) Culture conditions: optimal cell concentration, culturing time, confluency, cell number, cell viability, b) cell identity: cell markers expression, cells morphology analysis, c) cellular behaviours: migration, cellular interactions. Results were obtained by imaging on Nikon Ti-2 microscope and the images were analysed on Nikon NIS-Elements software. Statistical analysis was conducted on Prism Graphpad.
Results. The correlation between seeding densities and cell viability with cell culture time were clearly established. A panel of cell surface marker was defined based on positive and negative selection makers that are differentially expressed by both cell types. A scratch assay was conducted to study the migration and cell interaction.
Conclusion. The study optimised the workflow and culture conditions for all projects exploring OECs and fibroblasts. The outcomes greatly aid in development of an optimal cell cocktail for SCI therapy.

P10: Optimisation of growth factor testing on olfactory ensheathing cells

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Growth factors have different functions upon binding to receptors of target cell resulting in different effects such as changes in morphology or changes in metabolic rate. Further, growth factors have different concentration-dependent effective range. Since growth factors affect olfactory ensheathing cells (OEC) morphology, proliferation, and migration, discovering specific concentrations and growth factor combination can improve our spinal cord injury treatment by modulating OEC behaviour and activity. Therefore, the aim of this study is to optimise growth factor testing on olfactory bulb derived OECs in 2D and 3D to determine the effects of different growth factor concentrations on cellular activity and morphology.
384-well plates have been used for 2D analysis of effects of different growth factors and their concentration on mouse-derived bulb OEC morphology and cell activity using resazurin assay and confocal microscopy. Mouse-derived bulb OEC spheroids have been used to analyse effects of growth factor concentrations on cell migration in 3D using 3D printed device and confocal microscopy. Statistical analysis is performed using GraphPad Prism and R.
Analysis of growth factor treatment of bulb OECs in 2D show changes in cell activity measured by changes in fluorescence intensity of metabolised when comparing control to treatment groups. Some growth factors also show affect cell shape significantly compared to untreated bulb OECs in a concentration dependent manner based on p-values when comparing control to treatment groups. OECs leaving spheroid show potentially increased migration towards specific growth factor concentration gradient using a specifically designed 3D device.
This study shows that the optimised protocol shows effects of growth factor concentrations on OEC morphology and activity in 2D, and cell migration in 3D. However, the main limitation is that resazurin assay is unable to detect fine changes in cellular activity.

P11: Human tyrosinase inhibitors from natural resources as potential cure for skin hyperpigmentation

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Several treatments for skin pigmentation are available today, however, many have unwanted side effects. Classic drugs like hydroquinone, arbutin, mequinol and kojic acid have been considered strongly carcinogenic, with related adverse effects. Tyrosinase is a rate-limiting enzyme during the melanin synthesis process. Tyrosinase inhibitors can be a potential cure for hyperpigmentation. According to the literature, mushroom tyrosinase assay provided a quick and convenient method to screen for inhibitors among natural materials. However, many of the mushroom tyrosinase inhibitors were not effective against human tyrosinase. Therefore, the aim of this project is to develop robust cell-free tyrosinase assays using mammalian cell line lysates. Additionally, the assays will be used to test the extracts and fractions of selected natural resources based on previous literature research and mushroom tyrosinase assay results. Isolation and structure elucidation of human tyrosinase inhibitors will be investigated and the activity of the compounds will be corfirmed by cell-free tyrosinase assays developed.

P12: Investigation of pneumococcal strains from infant nasopharyngeal samples

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Acute respiratory infections (ARIs) occur throughout life but are most common during the first two years. They are the leading cause of death in children aged under 5-years, and the sixth leading cause of death for all ages globally. One of the most common bacterial pathogens responsible for ARIs is Streptococcus pneumoniae (Spn). The aim of this study was to investigate the dynamics of pneumococcal nasopharyngeal carriage using multilocus sequence typing (MLST) to determine the sequence types (ST) within a subset of pneumococcal-positive nasal swabs from children. A subset of pneumococcal positive swabs was selected from 19 children (isolated weekly over at least 4 weeks as part of the Brisbane-based Observational Research in Childhood Infectious Diseases birth cohort). PCR and sequencing of 7 pneumococcal MLST genes was performed using standard pneumococcal MLST primers. MLST analysis identified 15 distinct pneumococcal STs, with 4 STs (ST156, ST1373, ST63, ST1262) making up 62% of all swabs. Various patterns of pneumococcal carriage were seen in children over time. For example, subject 027 had Spn ST156 for three consecutive weeks, then the nasal swab collected three weeks later showed Spn ST1373, which persisted for 12 weeks. Subject 085 also had Spn ST1373 for three consecutive weeks. Subject IDs 015, 098 and 157 had colonisation with Spn ST63 for a combined total of 12 weeks, making it the second most prevalent ST after ST1373. Subject IDs 109 and 150 had 7 and 9 weeks of confirmed colonisation with Spn ST1262, respectively. Overall, our data suggests that pneumococcal carriage with the same strain persists over several weeks, although temporal shifts do occur in pneumococcal STs. The detailed analysis of pneumococcal carriage may assist in the development of future treatment and prevention strategies.

P13: Discovery Biology: Image-based drug discovery for protozoan pathogens

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Chagas Disease, Leishmaniasis and Malaria are human diseases caused by protozoan pathogens. These diseases collectively affect >250 million people per year, in over 100 countries, and result in >667K deaths annually. Available treatments for these diseases have generally been shown to have adverse side effects, variable treatment efficacy or have resulted in drug resistance, thus identification of new compounds for the drug discovery pipeline are critical. Discovery Biology undertakes research in collaborative not-for-profit and academic based drug discovery consortiums for these diseases, which has led to identification of compounds with translatable in vivo activity and new drug candidates that have progressed to clinical trials.

To support our drug discovery research, we have three automated, high-end confocal imaging systems for high-throughput screening (HTS), several automated liquid handling devices, large imaging data storage and analysis capability and significant in-house expertise. High-content in vitro assays in 384-well format have been established for these parasites to detect intracellular or intraerythrocytic infection, using single or multiparametric read-outs. High-quality image acquisition, analysis and associated script development interfaces facilitate accurate evaluation of the impact of compounds on parasite growth and development over time, through multiple life cycle stages and across numerous parasite strains. We have also developed methods to identify replicating intracellular Trypanosoma cruzi parasites, utilising the nucleoside analogue 5-ethynyl-2’-deoxyuridine, to determine the impact of replication on compound activity. For each assay, multiple factors are considered, including host and parasite health; application of fluorescent dyes to identify and distinguish parasites and host cells; and linearity of infection and detection.

Our expertise in assay development and optimisation, HTS, hit identification and hit-to-lead optimisation has significantly impacted protozoan drug discovery and research, including multiple malaria and one leishmaniasis drug candidate, with > 140 publications in assay development, HTS, hit-to-lead, and lead optimisation in protozoan drug discovery.

P14: Characterizing the role of miR-34a-5p in natural killer cell activation against cancer cells

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Natural killer (NK)-cells are immune effector cells that lyse cancer cells and infected cells without prior activation. Developments in immunotherapeutic approaches have led to a resurgence in targeting NK-cells in cancer immunotherapy. A number of cell surface receptors and transcriptional factors are known to control NK-cell activation. Yet little is known about regulatory molecules involved in NK-cell anti-tumoral function. microRNAs (miRNA) are small non-coding RNAs able to regulate ~60% of human genes and have critical impact on biological functions. We developed an integrated systems analysis of miRNA target network that affects anti-tumoral immunity of NK-cells. Transcriptomic analysis of two activation systems: direct cytotoxicity and antibody-dependent cell-mediated cytotoxicity revealed a strong negative correlation between mRNAs and miRNAs during both activation conditions. The putative miRNA- gene network associated with NK-cell activation identified miR-34a-5p as a major regulatory hub binding to 3'UTR of several genes with significantly enriched target sites. We further observed and independently validated the levels of miR-34a-5p are reduced in activated NK-cells compared to resting cells. Additionally, we provide evidence of miR-34a-5p-dependent cytokine release in NK-cell activation. This work demonstrates that miR-34a plays a critical role in the regulation of the NK-cell activation and potentially enhances NK cell anti-tumoral efficacy opening new avenues for miRNA-based immunotherapies.

P15: Antimicrobial metabolites of Bacillus Probiotics

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Antimicrobial resistance is caused by the misuse of antibiotics in livestock. A safer alternative can be found in probiotics, which inhibit pathogen growth and also releases a range of nutrients to help rebalance the microbiota compared to antibiotics. Concerns have arisen over probiotic lack of survival within the upper gastrointestinal system, which has generated interest into the use of spore-forming probiotics such as Bacillus. Bacillus probiotics form a self-protecting layer, which can survive the harsh conditions of the upper gastrointestinal system, and subsequently enter the small intestine to release a range of health promoting metabolites. Although the current literature has identified several metabolites and their mechanisms, the majority remain unidentified and further research is needed to optimize their performance for industrial use. My project tackles two main issues: what are the metabolites responsible for their antimicrobial activity; and what are their exact mechanisms of action. Assisting in tackling these issues as an industry partner is Bioproton, a leading agricultural company specializing in animal feed. The results of my project will assist in screening for future antimicrobial probiotics and will reveal further avenues to optimize their performance.

P16: NMR-based metabolomics to decipher the metabolic consequences of alcohol catabolism in cerebrospinal fluid

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Studies have shown that alcohol and/or its metabolites are metabolised in the brain, suggesting that alcohol metabolism in vivo and the resulting CSF chemistry changes increase neurotransmitter concentrations. The purpose of this study is to quantify CSF metabolite concentration changes over 3-4 hours, as ethanol was slowly administered into weanling piglets to achieve a blood alcohol level of 40-50 mM. We measured the 1H NMR-spectra (900 MHz) of Cisterna magna CSF samples, taken at 20-40 minute intervals, during ethanol infusion and after. The metabolites in the sample were identified and their concentrations determined. Results showed that most of the metabolites, including glutamine, increased in concentration as ethanol increased in concentration. However, as ethanol began to decrease in concentration so too did many of the identified metabolites (e.g., glutamine and 2-oxoglutarate). This aligns with a previous hypothesis in which alcohol dehydrogenase activity and the resulting NADH accumulation interfered with energy metabolism. This study proposes that the accumulation of NADH results in NADH product inhibition. In which ethanol conversion to acetaldehyde and then to acetate utilises NAD+, therefore creating an increase in NADH and a decrease in NAD+ (increasing NADH/NAD+ ratio). This leads to an accumulation of metabolites, interfering with many of the metabolic pathways, most noticeably the Krebs Cycle. This suggests that other CSF chemistry changes play a role in this effect, as a result of alcohol being metabolised in the brain.

P17: Deciphering the role of Carbonic anhydrase III in promoting cancer patient survival

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Carbonic anhydrase III (CA III) is a metalloenzyme encoded by CA III gene in human cells. Carbonic anhydrases usually act as pH regulator in cells, while CA III shows a significantly low activity as a pH regulator. However, CA III was reported to be an antioxidant. Antioxidants can regulate cellular redox homeostasis by reacting with reactive oxygen species and antioxidants can often protected cells from oxidative stress and induce cell proliferation. Therefore, antioxidants often lead to a bad prognosis for cancer patients. Two surface exposed cysteine residues can be glutathionylated and are related to the antioxidant function of CA III. Cysteine residues in proteins can undergo oxidative modification, which might activate of deactivate the enzyme. CA III is highly expressed in many highly metabolic tissues, especially in muscle. Cancer cells are often highly metabolic, but CA III expression have great variations between different types of cancer. CA III is most upregulated in brain cancer and most downregulated in breast cancer. Although CA III has antioxidant functions, higher CA III expression is related to a good prognosis for cancer patients. Thus, beside its antioxidant function, CA III is related to other unknown mechanisms that provide protective advantages for cancer patients. With a high expression level in normal muscles, CA III was found poorly expressed in muscles of myasthenia patients. CA III can directly interact and inhibit Bcl2-Associated Athanogene 3 (BAG3). BAG3 participated in autophagy that will worsen the disease. The decrease of CA III expression in myasthenia patients results in the upregulation of autophagy, which will lead to a bad prognosis for myasthenia patients. It was also found that overexpression of BAG3 is related to a bad prognosis for cancer patients. Therefore, CA III possible can inhibit BAG3 in cancer cells and lead to a good patient prognosis.

P18: Prognostic utility of circulating tumour cells from head and neck cancer patients

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Atherosclerosis which is the main underlying reason for cardiovascular diseases, is caused by the build-up of cholesterol and fats on the arterial walls. The process for the atherosclerotic plaque formation involves chronic inflammation driven by the oxidation of low-density lipoproteins (LDL) by the macrophages in the damaged vascular. Despite being responsible for millions of deaths each year, current treatment options available are unable to keep up with the rise of cases caused mainly due to poor diet and lack of exercise. The current pharmacological treatments only treat the risk factors of the disease which include hypercholesterolemia, hypertension, and hyperglycaemia. Surgical treatments are performed for severe cases however they pose the risk of perioperative and post operative complications. Nanomaterial mediated drug delivery is a novel approach for the treatment of atherosclerosis that has been generating interest over the past few years. Nanoparticles offer site specific release of drugs to the diseased vascular for therapeutic purposes, or aid in the diagnosis of the disease by attaching an imaging agent to the nanoparticle or have both effects for a theranostic approach. There are many types of drugs classes that are being used for the treatment of atherosclerosis, classified into hydrophobic and hydrophilic drugs. One of the main problems faced by hydrophobic drugs is their poor water solubility which decreases the bioavailability of the drug. In this project, we use the polymer polysuccinimide (PSI) to synthesise polymeric nanoparticles which could encapsulate hydrophobic drugs. Furthermore, PSI can be aminolysed to form a derivative of polyaspartic acid, which allows for easy modifications to the polymer backbone, allowing for the binding of targeting ligands or diagnostic agents. This polymer is both biocompatible and biodegradable making it an ideal candidate for a drug delivery system. This polymer is both biocompatible and biodegradable making it an ideal candidate for a drug delivery system.

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