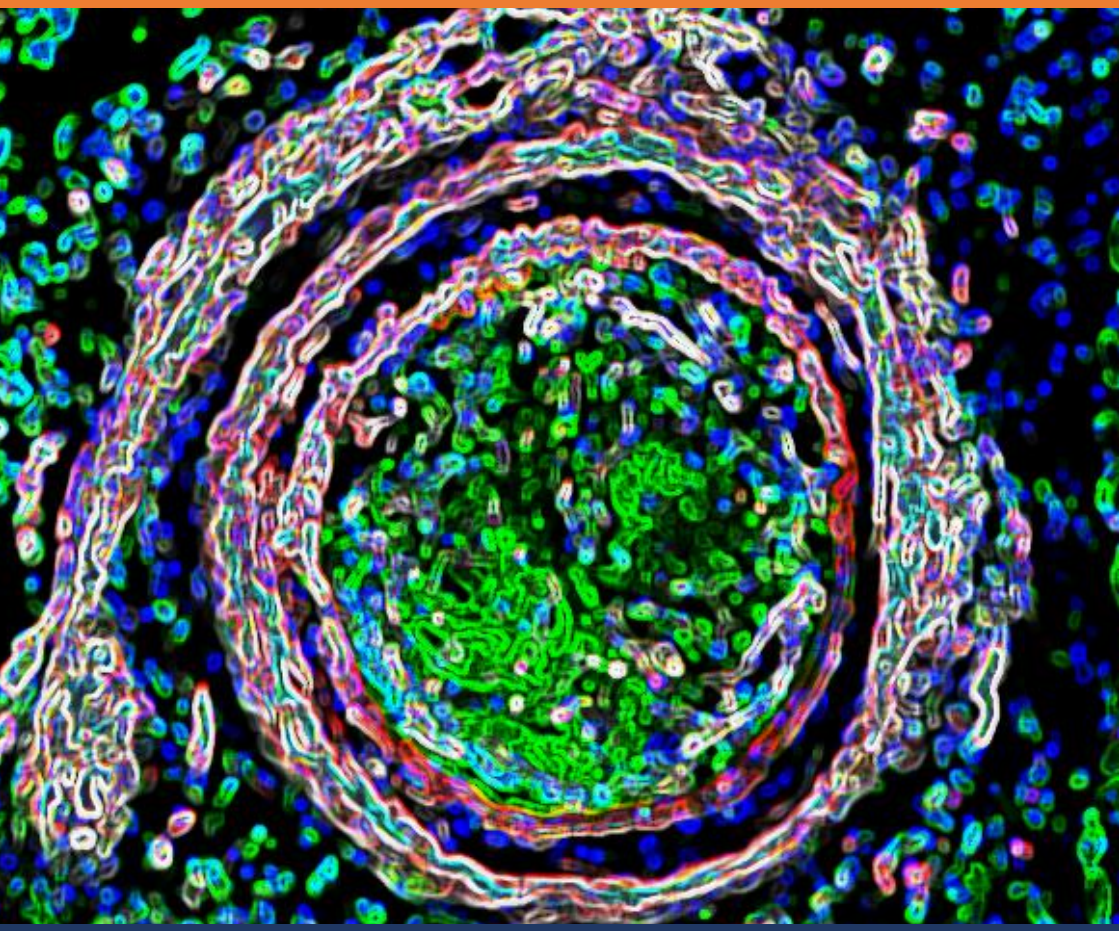
10TH ANNUAL BIOMEDICAL SCIENTIFIC CONGRESS 2022



Building Science Foundations for Translational Medicine

ABSC 2022
10TH ANNUAL BIOMEDICAL SCIENTIFIC CONGRESS

Building Science Foundations for Translational Medicine

21 Sept 2022: CONFERENCE DAY
22 Sept 2022: CAREER DAY

VENUE: NUS MD11, CRC Auditorium

Organized by

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Welcome Message

Prof Chong Yap Seng

Lien Ying Chow Professor in Medicine
Dean, NUS Medicine

Dear Delegates and Partners of ABSC 2022,

Since the biomedical industry became Singapore's fourth pillar of the economy in 2000, the biotechnology sector has expanded considerably, with the number of biotech startups increasing every year. The growth of the sector was further propelled by the Covid-19 pandemic, with homegrown companies developing diagnostic tests for the disease while multinational pharmaceutical companies established vaccine manufacturing facilities here.

In order for the biomedical industry to continue its growth trajectory, we need more projects to succeed in their translational journey. Many biomedical observations with scientific potential do not progress to become biotech solutions. Even if projects do succeed like in the case of MiRXES, it is a tremendously long journey. How can we innovate to solve challenges plaguing translational medicine and science? What can we do to shorten the translational process? Can we collaborate better with professionals not in healthcare and with the international research community? What can we do better to deliver on the promise to meet healthcare needs of populations through translational research?

It is therefore timely that the theme for the 10th the Annual Biomedical Scientific Congress is "Building Science Foundations for Translational Medicine". Impetus for critical, life-saving and meaningful biomedical research that translates well cannot depend on momentum generated by pandemics. We need to be ahead of the curve.

I wish everyone an enriching and fruitful symposium.

Thank you.

Welcome Message

A/Prof Kevin Tan

Associate Professor
Laboratory of Molecular and Cellular Parasitology
Head
Department of Microbiology and Immunology
Vice-Dean of Graduate Studies
NUS Medicine

Dear graduate students, postdoctoral fellows and colleagues,

It gives me great pleasure to welcome you to the 10th Annual Biomedical Scientific Congress (ABSC). The two-day congress is a signature event for our graduate student and postdoc community. On our 10th anniversary, the NUS Medicine Graduate Student Society (GSS) has planned an exciting and enriching programme for you.

The scientific congress will feature globally recognized researchers, including a Nobel laureate, who will showcase cutting-edge research in material science, infectious diseases, cancer, cardiovascular disease, and ageing. The career day will feature expert panels on career development as well as a networking event that will bring together academics, industry professionals, and students to mingle and discuss various career paths and prospects.

The theme for this year's ABSC, 'Building Science Foundations for Translational Medicine', underscores the importance of fundamental research as a foundation for impactful translational research. I hope you will keep this principle in mind as you enjoy the scientific talks featured in this congress.

I would like to thank the NUS Medicine GSS for organizing this special event for the graduate student and postdoc research community. In particular, my thanks go out to Faizus Sazzad, Weirui Zhang, Caroline Robert, Jessica Lu, Samira Sadeghi and Previtha Dawn for leading this initiative. We mustn't forget Geetha Warrier and Yumi Li for providing administrative support to the committee and A/Profs Zhang Yongliang and Polly Chen for serving as faculty advisors.

I wish you a rewarding time at our 10th ABSC!

Foreword

Dr Faizus Sazzad

President-Elect
NUS Medicine Graduate Students' Society
***Chairperson**, 10th Annual Biomedical Scientific Congress 2022*

Dear Professors, Friends and Graduate Students

It is an absolute honour for me to welcome you to the 10th Annual Biomedical Scientific Congress (ABSC 2022). We are pleased to host you in person this year, despite being challenged by the global health emergency unleashed by the COVID-19 pandemic in the previous years.

The legacy of ABSC is very much known among this community. The congress has always aimed to promote inter-professional collaboration, translational medicine research and education within NUHS and participating departments. This year our prime focus is on building science foundations. We hope this platform will foster new ventures and avenues for collaboration and enrich our research skills.

I hope you will enjoy the scientific discussions and participate in the abstract presentations to showcase your own research capabilities as well as interact substantially with your fellow researchers. The unique career day sessions will be led by panelists from academia, grantors, industry and sponsors, who can interact with you, guide your career and enlighten you for your future career aspirations. In addition, the "Networking Dinner" night will provide an interactive gathering between promising graduate students and potential employers.

I would like to extend my gratitude to all members of the ABSC organizing committee for their continuous support and relentless hard work, especially Jessica Lu, Samira Sadeghi, Weirui Zhang, and Previtha Dawn. I want to thank A/Prof Kevin Tan and A/Prof Heng Chew Kiat and the advisory panel A/ Prof Polly Leilei Chen and A/Prof Zhang Yongliang, for their valuable advice throughout the planning of this congress. As a team, we remain grateful to DGS administrators, namely Geetha Warrier and Yumi Li Cuiyu, our valuable sponsors, panelists, chairpersons, speakers, judges, moderators and all participants for making this event successful.

I remain thankful and look forward to seeing you at our events.

Sponsors

This congress has been made possible by the generous support of our sponsors. We express our heartfelt gratitude to the following companies for sponsoring and supporting our event.

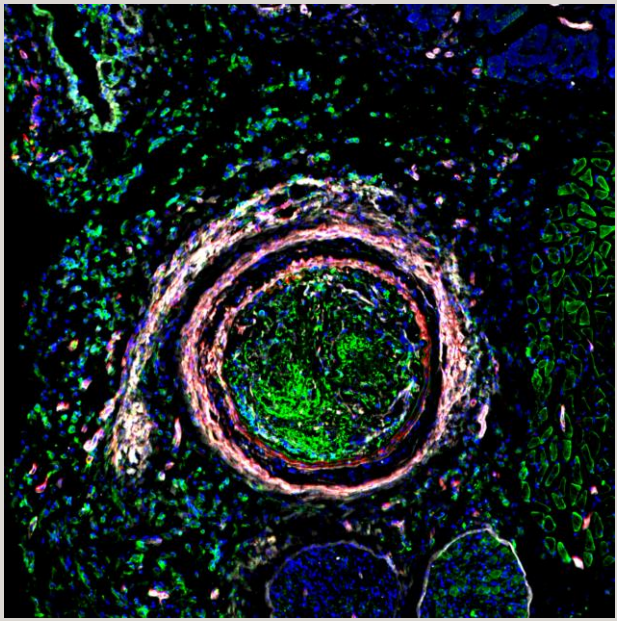
ThermoFisher SCIENTIFIC

Lonza

Singleron

SCIENCEWERKE

Photo Contest Winners

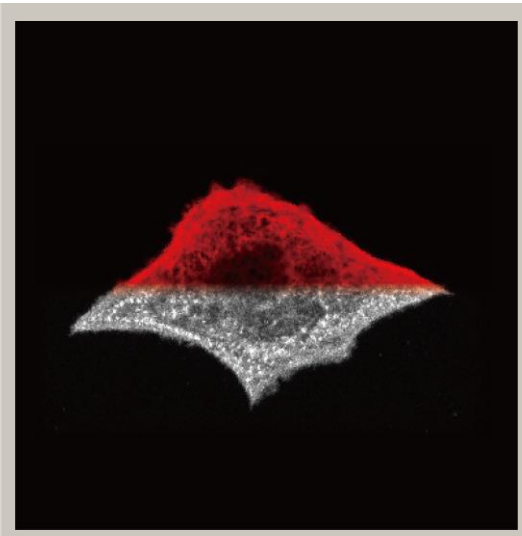


First Place: The Death Spiral of Inflammation
Owen Ang

Graduate Student (PhD)
Immunology Translational Research Programme

This image encapsulates the process of a carotid artery recovering from a wire denudation procedure, which caused extensive occlusion of the arterial lumen due to accumulation of inflammatory immune cells and blood cells coming from all directions. If left unresolved, the arterial blockage will persist, leading to stoppage of blood flow. This process visually mimics the widely known ant mill (or death spiral) phenomenon which often ends with the death of the ant colony.

Photo Contest Winners

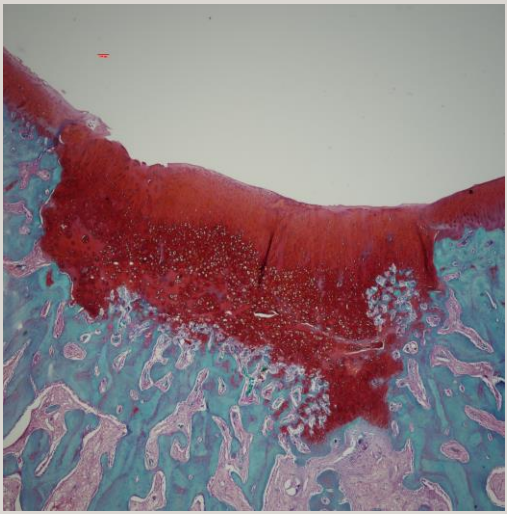


Second Place: The Shape of My Heart

Yike Zhu

Research Fellow
Cardiovascular Disease Translational Research Programme

This is immunofluorescence image of a de-differentiating adult mouse cardiomyocyte in culture, with a shape reminiscent of Singapore map. The combined red and white channels represent the two colors in the national flag of Singapore. The top red channel is alpha-actinin, while the bottom grey channel is cardiac troponin I. As one of the most terminally differentiated cells in the body, cardiomyocyte de-differentiation is a key precedent process of proliferation and heart regeneration.



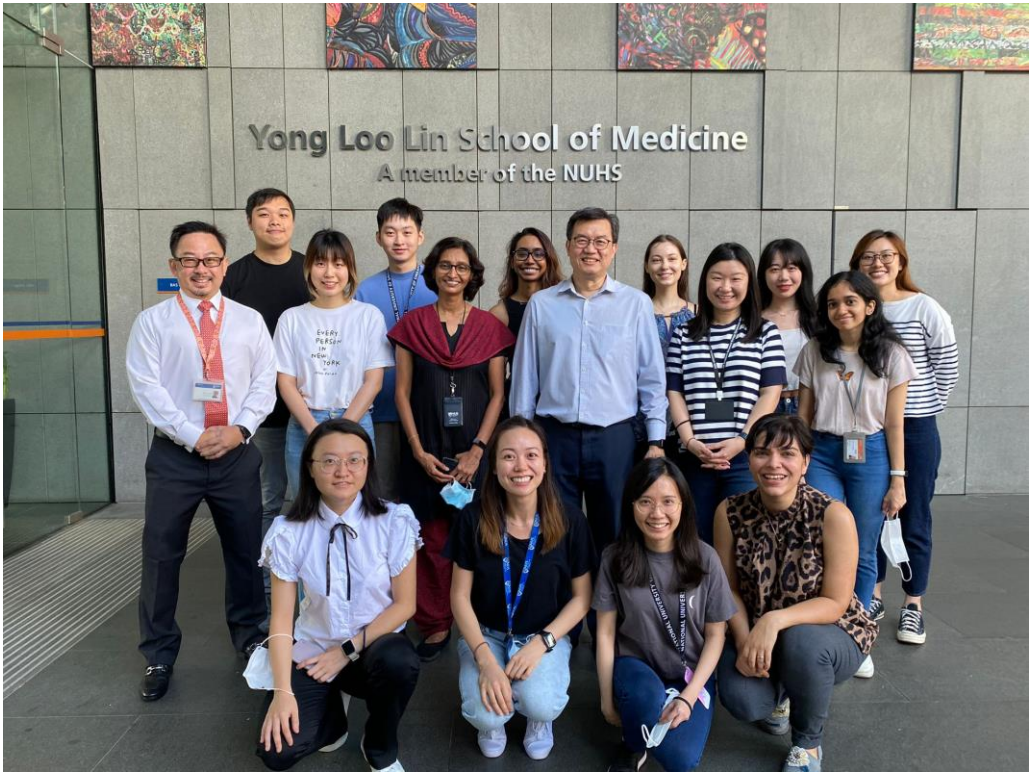
Third Place: Cartilage Repair after Pulsed Electromagnetic Field Stimulation

Goh Shu Lin, Doreen

Medicine Student (MBBS)
Department of Orthopaedic Surgery and Intercalated Year Programme (IYP) MSc Candidate

Samples were harvested from an in vivo osteochondral defect rabbit model 6 weeks after pulsed electromagnetic field stimulation. After embedding and sectioning, samples were stained with Safranin O to demonstrate sulfated glycosaminoglycan (sGAG) deposition. In this microscopic image, the defect is entirely filled with sGAG-positive cartilaginous material and chondrocytes nested within lacunae.

ABSC Committee 2022



Front row (left to right): *A/Prof Kevin Tan, Weirui Zhang, Geetha Warrier, A/Prof Heng Chew Kiat, A/Prof Polly Leilei Chen and Mugdha Patwardhan*

Front (kneeling, left to right): *Mengqi Shi, Jessica Lu, Tay Hui Yi and Samira Sadeghi*

Back row (left to right): *Jonathan Lim, Tianzhi Zhao (Richard), Previtha Dawn, Marie Beatrix Kruth, Liuyun Wu and Vivian Tan*

ABSC Committee 2022

Faculty Advisors

A/Prof Zhang Yongliang
A/Prof Polly Leilei Chen

Administrative Staffs

Geetha Warrier
Yumi Li Cuiyu

Chairperson

Faizus Sazzad

Congress Secretary

Vivian Tan

Design & Publicity

Caroline Robert (Lead)
Director of Community Affairs

Rhonda Chee
Publicity Secretary

Liuyun Wu
Graduate Student Representative

Registration & Logistics

Jessica Lu (Lead)
General Secretary

Mugdha Vijay Patwardhan
Assistant General Secretary

Jonathan Lim
Creative Secretary

Sponsorship

Samira Sadeghi (Lead)
Treasurer

Marie Beatrix Kruth
Business Manager

Tianzhi Zhao (Richard)
Marketing Officer

Scientific Events

Previtha Dawn (Lead)
Director of Student Affairs

Vivian Tan
ABSC Congress Secretary

Tay Hui Yi
Welfare Secretary

Mengqi Shi
Scientific & Career Affairs Secretary

Career Events

Faizus Sazzad (Lead)
President, NUS Medicine GSS

Weirui Zhang
Vice-president, NUS Medicine GSS

ABSC Judges

Abstract Judges

A/Prof Polly Leilei Chen

A/Prof Heng Chew Kiat

A/Prof Zhang Yongliang

Oral Presentation Judges and Session Chairs

Prof Roger Foo

A/Prof Gan Yunn Hwen

A/Prof Heng Chew Kiat

A/Prof Zhang Yongliang

A/Prof Polly Leilei Chen

A/Prof Raymond Seet

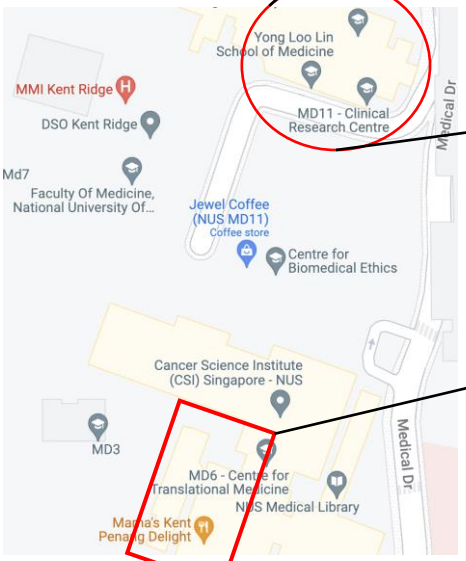
Lightning Talk Judges

Prof Wee Joo Chng

A/Prof Zhi Xiong Chen

A/Prof Kevin Tan

Guide Map

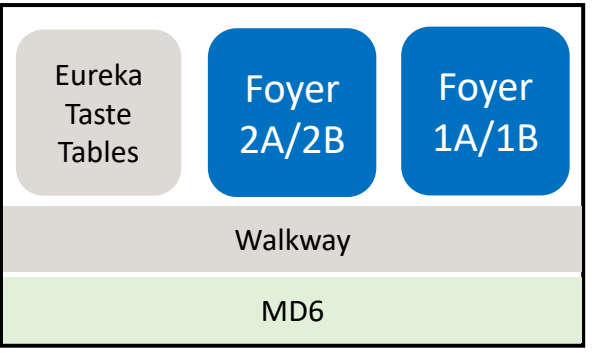


Sessions & Talks; Registration

NUS MD11

CRC Auditorium (Level 1)

10 Medical Dr,
Singapore 117597



Student Posters, Sponsor Booths, Food & Refreshments

NUS MD6

Foyers 1A/1B and 2A/2B

14 Medical Dr,
Singapore 117599

ABSC Programme

ABSC Programme

DAY 1 – 21st Sept 2022

Day 1: 21st Sept 2022 (Wed)	
08:30 – 08:45	Registration (MD11 Foyer)
8:45	Room opens and house rules (CRC Auditorium, MD11)
08:50	**Welcome address** **A/Prof Kevin Tan** Head, Department of Microbiology & Immunology Vice-Dean (Graduate Studies), NUS Medicine
Scientific sessions (CRC Auditorium, MD11)	
Session 1 (9:00 – 10:30)	
9:00 – 10:00	**Keynote talk:** Unfolding the Misfolded: Cardiac Amyloidosis **Prof Ronglih Liao** Co-Director of the Stanford Amyloid Center, Professor of Medicine at Stanford University School of Medicine **Chairperson** **Prof Roger Foo** Zayed bin Sultan Al Nahyan Professor in Medicine, NUS Medicine **Moderator:** Faizus Sazzad
10:00 – 10:15	**Oral presentation-1** : Genome-Wide CRISPR Screen Identifies an NF2-adherens Junction Mechanistic Dependency for Cardiac Lineage **Speaker:** Lee Chang Jie Mick
10:15 – 10:30	**Oral presentation-2:** Identification of Causal Non-coding Genetic Variants Linked to Cardiac Function **Speaker:** Zhang Weirui
10:30 – 11:00	**Tea break and Poster session 1 (MD6 Foyer 2A-B)**
Session 2 (11:00 – 12:05)	
11:00 – 11:35	**Scientific talk:** Upstream Regulation of Wnt Signaling: Biology and Therapy **Prof David Virshup** Program Director for Cancer & Stem Cell Biology, Duke-NUS Graduate Medical School

ABSC Programme

DAY 1 – 21st Sept 2022

	Chairperson **A/Prof Polly Leilei Chen** Principal Investigator, Cancer Science Institute of Singapore Associate Professor, Department of Anatomy, NUS Medicine **Moderator:** Clara Koh
11:35 – 11:50	**Oral presentation-3:** A Balancing Act of the RNA Editing Enzyme ADAR1 in the Liver: Immune Sensing and Suppression **Speaker:** Gan Wei Liang
11:50 – 12:05	**Oral presentation-4:** GSTT2 and the Response to BCG Immunotherapy **Speaker:** Mugdha Patwardhan
12:05 – 1:45	**Lunch break and Poster session 2 (MD6 Foyer 2A-B)**
Session 3 (1:45 – 3:05)	
1:45 – 2:20	**Scientific talk:** Genetic Glycoengineering in Bacteria **Dr Chris Sham** Assistant Professor, Department of Microbiology and Immunology, NUS Medicine **Chairperson** **A/Prof Gan Yunn Hwen** Associate Professor, Department of Biochemistry, Co-Director, Infectious Diseases Translational Research Program, NUS Medicine **Moderator:** Tay Hui Yi
2:20 – 2:35	**Oral presentation-5:** Investigating the Role of Rab11a During Enterovirus 71 Infection **Speaker:** Ng Qing Yong
2:35 – 2:50	**Oral presentation-6:** Red Blood Cell-derived Extracellular Vesicles Display Endogenous Anti-viral Properties and Serve as Effective Oligonucleotide Carriers for SARS CoV-2 Therapy **Speaker:** Migara Kavishka Jayasinghe
2:50 – 3:05	**Oral presentation-7:** Role of CD151 in Influenza-induced Asthma Exacerbation (IAE). **Speaker:** New Chih Sheng
3:05 – 3:35	**Tea break and Poster session 3 (MD6 Foyer 2A-B)**

ABSC Programme

DAY 1 – 21st Sept 2022

Session 4 (3:35 – 4:55)	
3:35 – 4:10	**Scientific Talk:** Longevity Medicine: The Path towards Prevention **Prof Andrea Maier** Oon Chiew Seng Professor in Medicine Co-Director of Centre for Healthy Longevity, NUS Medicine **Chairperson** **A/Prof Raymond Seet** Associate Professor, Department of Medicine, NUS Medicine **Moderator:** Caroline Robert
4:10 – 4:25	**Oral presentation-8:** Narciclasine Promotes Lipolysis and White Fat Browning in Diet-induced Obese Mice **Speaker:** Belinda Ong
4:25 – 4:40	**Oral presentation-9:** Predicting Individual Brain Regional Atrophy Progression and Cognitive Decline Using Functional Connectome **Speaker:** Yu Xiao
4:40 – 4:55	**Oral presentation-10:** Low Plasma Ergothioneine Levels are Associated with Neurodegeneration and Cerebrovascular Disease in Dementia **Speaker:** Liuyun Wu
Plenary Session (4:55 – 5:45)	
4:55 – 5:40	**Plenary talk** Materials of the Future **Prof Sir Konstantin Novoselov** Director, the Institute for Functional Intelligent Materials, NUS Nobel Laureate, Royal Society Research Fellow, Distinguished Professor of Materials Science and Engineering, NUS **Chairperson** **A/Prof Heng Chew Kiat** Department of Paediatrics, NUS Medicine **Moderator:** Caroline Robert
5:45	**Announcement: Winners of the oral and poster presentation**
6:00	**Day closing**

ABSC Programme

DAY 2 – 22nd Sept 2022

Day 2: 22nd Sept 2022 (Thu)	
09:30 – 10:00	Registration (MD11 Foyer)
10:00	**Welcome address** **Faizus Sazzad** Chairperson, ABSC 2022 President-Elect, NUS Medicine GSS
Career sessions (CRC Auditorium, MD11)	
Session 1 (10:05 – 11:00)	
10:05 – 11:00	Theme: **Ace Your Research in Academia** **Panelists** • **Prof Wee Joo Chng** Vice-Dean (Research), NUS Medicine • **A/Prof Zhi Xiong Chen** Assistant Dean (Education), NUS Medicine • **A/Prof Kevin Tan** *Head, Department of Microbiology & Immunology* *Vice-Dean (Graduate Studies), NUS Medicine* **Moderator** Vivian Tan
11:00 – 12:00	**Lightning talks**
12:00 – 1:00	**Lunch break (MD6 Foyer 2A-B)**
Session 2 (1:00 – 2:00)	
1:00 – 2:00	Theme: **Break into the Fast-tracked Biomedical Industry** **Panelists** • **Dr Shu Wen Koh** Director, NUS Industry Liaison Office (ILO) • **Dr William Tan** Associate Director Medical Affairs, MiRXES • **Ms Ashley Wittorf** APAC Head of Business Development, Johnson & Johnson • **Dr Sashi Kesavapany** Director, Biomedical Science, SGInnovate **Moderator** Faizus Sazzad

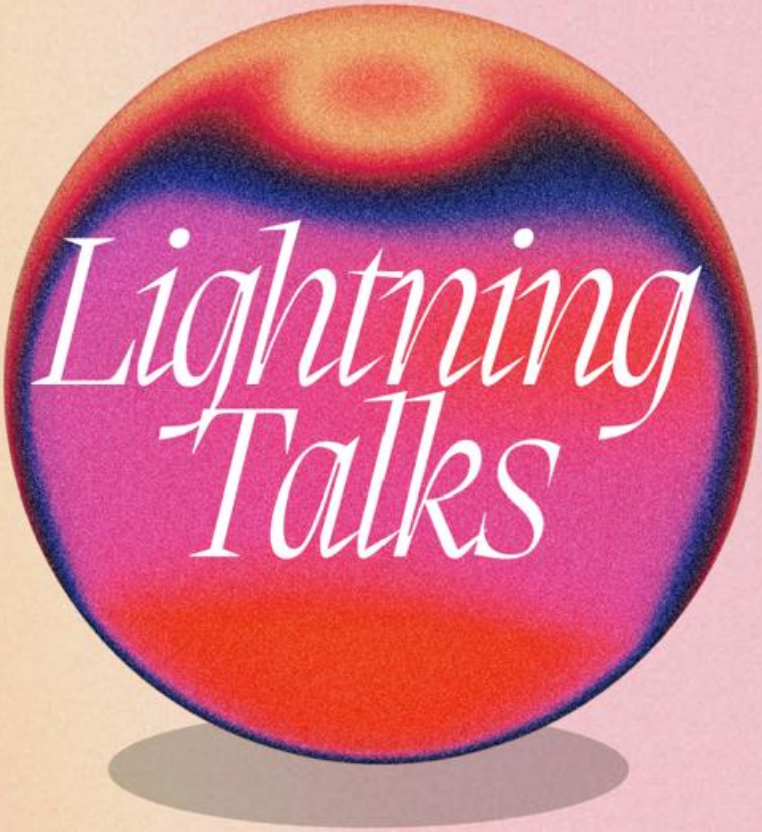
ABSC Programme

DAY 2 – 22nd Sept 2022

Session 3 (2:00 – 3:15)	
2:00 – 3:15	Theme **From Lab Bench to Store Shelves** **Panelists** • **Prof Lawrence Khek-Yu Ho** Director, Centre for Innovation in Healthcare, NUHS • **Dr Siang Lin Yeow** Head (Enterprise), National Health Innovation Centre Singapore (NHIC) • **Dr Ajith Isaac** Investment Manager, STRIVE, Pre-Seed - Seed stage enablers • **Dr Pei She Loh** Ex-Chairperson, ABSC Congress 2021, R&D Consultant , AVECRIS **Moderator:** Weirui Zhang
3:15 – 3:45	**Tea break (MD6 Foyer 2A-B)**
Session 4 (3:45 – 4:55)	
3:45 – 4:55	Theme **Unlock Your Leadership Potential** **Panelists** • **Dr Xian Jun Loh** Executive Director, Institute of Materials Research and Engineering, A*STAR • **Ms Annie Lim** Vice President Human Resources at Hummingbird Bioscience • **Prof Roger Foo** Zayed bin Sultan Al Nahyan Professor in Medicine, NUS Medicine • **Dr Juliana Chan** CEO, Wildtype Media Group **Moderator** Previtha Dawn
4:55	**Announcement: Winners of the lightning talks**
5:00	**Day closing**

NUS Medicine GSS Presents

10th ABSC 2022



3MT LIVE PRESENTATION BY GRADUATE STUDENTS!

3 MIN ON-STAGE PRESENTATION: HIGHLIGHT YOUR RESEARCH IN THIS ADDITIONAL PLATFORM TO SHOWCASE YOUR CONTRIBUTIONS.

VENUE: CRC AUDITORIUM, MD11.
DATE: 22 SEPTEMBER 2022. TIME 10AM-12PM.

Lightning Talks

DAY 2 – 22nd Sept 2022

11:00 – 12:00	Lightning Talks (CRC Auditorium, MD11)
11:00 – 11:10	**Lightning talk-1** **Title:** Elucidating the Role of ADAR1 in Regulating Immunotherapeutic Response in Multiple Myeloma **Speaker:** Koh Mun Yee
11:10 – 11:20	**Lightning talk-2** **Title:** Androgen-Dependent Tissue Factor Pathway Inhibitor-regulating Protein (ADTRP) Regulates Adipogenesis, Glucose metabolism and Inflammation Associated with Obesity and diabetes **Speaker:** Ong Sze Min
11:20 – 11:30	**Lightning talk-3** **Title:** A Concerted Increase in Intron Retention and Readthrough Drives Transposon Expression During Aging and Senescence **Speaker:** Kamil Pabis
11:30 – 11:40	**Lightning talk-4** **Title:** Making Bioprinting One-step Closer to Translational Application – Capillary Vessel Printing by Interfacial Polyelectrolyte Complexation **Speaker:** Chixuan Liu
11:40 – 11:50	**Lightning talk-5** **Title:** The Impact of Yo-yo Dieting on Cardiac Health **Speaker:** Wang Xiao
11:50 – 12:00	**Lightning talk-6** **Title:** The Role of Long Non-coding RNA VENTHEART in Cardiomyocyte Differentiation and Maturation **Speaker:** Yang Yiqing
	Moderator Vivian Tan

NUS MEDICINE GSS PRESENTS

NETWORKING DINNER *night*

22ND SEPTEMBER 2022

6.30 PM ONWARDS

ENTRY: BY INVITATION

REGISTRATION

VENUE: DELLA & SENG GEE GUILD HALL
KENT RIDGE GUILD HOUSE, NUS

Networking Dinner

DAY 2 – 22nd Sept 2022

Day 2 – 22nd Sept 2022 (Thu)	
Venue:	**NUSS Kent Ridge Guild House**
6:30 – 7:00	Registration and seating
7.00 - 7:20	Guest of Honour **Prof Chong Yap Seng** *Lien Ying Chow Professor in Medicine* *Dean, NUS Medicine*
7:20 – 7:30	Ice Breaking Games
7:30 – 8:30	**Dinner and Networking**
8:30 – 9:00	**Prize Ceremony**
9.00 – 9:15	**Lucky Draw**
9:15 – 9:30	**Closing Address** **A/Prof Kevin Tan** *Head, Department of Microbiology & Immunology* *Vice-Dean (Graduate Studies), NUS Medicine*
9:30	**End of Events**

Meet Our Speakers!

Keynote Speaker

Prof Ronglih Liao

- *Professor of Medicine at Stanford University School of Medicine,*
- *Co-Director of the Stanford Amyloid Center,*
- *Visiting Professor of Medicine at Brigham and Women's Hospital, Harvard Medical School*

Ronglih Liao, PhD is co-Director of the Stanford Amyloid Center and Professor of Medicine at Stanford University School of Medicine. She is also a visiting Professor of Medicine at Brigham and Women's Hospital, Harvard Medical School. She was the first female Council Chair (2016-2018) of AHA Basic Cardiovascular Science Council.

Dr Liao has served numerous major leadership roles, with service to national and international societies, committees, and funding agencies, and as a committee member or reviewer. Moreover, Dr. Liao has continued her competitive independent investigation under direct research funding from the NIH continuously for over a decade. Over the years, Liao Lab has made critical contributions to the understanding of the molecule mechanisms that underlie the development of amyloid cardiomyopathy as well as the regulation of both cell fate and function in adult cardiac progenitor cells.

Keynote talk: Unfolding the Misfolded: Cardiac Amyloidosis

Plenary Speaker

Prof Sir Konstantin Novoselov

- *Nobel Laureate, Royal Society Research Fellow*
- *Distinguished Professor of Materials Science and Engineering, NUS*

Professor Sir Konstantin 'Kostya' Novoselov FRS joined the National University of Singapore on 8 April 2019 as Distinguished Professor of Materials Science and Engineering. A top physicist, he specialises in the area of condensed matter physics, mesoscopic physics and nanotechnology. Prof Novoselov is best known for isolating graphene at the University of Manchester, UK, in 2004, where he is Langworthy Professor of Physics and Royal Society Research Professor. He was awarded the Nobel Prize for Physics in 2010 for his achievements with graphene.

Prof Novoselov was born in Russia and holds both British and Russian citizenships. He graduated from the Moscow Institute of Physics and Technology and undertook his PhD studies at the University of Nijmegen in the Netherlands before moving to the University of Manchester in 2001. Prof Novoselov has published more than 300 peer-reviewed research papers, many of which are in top-tiered journals and with an h-index higher than 110.

He has been awarded numerous prizes, including the Nicholas Kurti Prize (2007), International Union of Pure and Applied Science Prize (2008), MIT Technology Review young innovator (2008), Europhysics Prize (2008), Bragg Lecture Prize from the Union of Crystallography (2011), the Kohn Award Lecture (2012), Leverhulme Medal from the Royal Society (2013), Onsager medal (2014), Carbon medal (2016) and Dalton medal (2016), among many others. He was knighted in the UK's 2012 New Year Honours.

Prof Novoselov was the first scientific director of the National Graphene Institute at the University of Manchester and sits on the International Scientific Advisory Committee of Australia's Centre for Future Low-Energy Electronics Technologies. He participated in the co- ordination and implementation of the European Graphene Flagship project – a €1 billion initiative of the European Commission.

Plenary talk: Materials of the Future

Scientific Speaker

Prof David Virshup

- *Program Director for Cancer & Stem Cell Biology (CSCB)*
- *Professor at Duke-NUS Graduate Medical School*
- *Professor of Pediatrics at Duke University in North Carolina*

Dr Virshup received his B.A. magna cum laude from Beloit College, majoring in chemistry. He received his M.D. from Johns Hopkins University in Baltimore, followed by clinical residency in Pediatrics and a fellowship in Pediatric Hematology/Oncology. He credits his research training and mentoring to William Zinkham, Vann Bennett, and Tom Kelly in the departments of Pediatrics, Cell Biology and Anatomy, and Molecular Biology and Genetics, all at Hopkins. Dr. Virshup established his first independent laboratory at the University of Utah in Salt Lake City, where over the course of 17 years he rose to Professor of Pediatrics and Oncological Sciences with an endowed chair as an investigator at the Huntsman Cancer Institute. He moved to Duke-NUS in Singapore in 2007 to help establish CSCB.

He has been elected to several honorific societies including the American Society for Clinical Investigation (ASCI), the American Association for the Advancement of Science (AAAS) and the Association of American Physicians (AAP). He is board certified in both Pediatrics and Pediatric Hematology/Oncology in the USA.

His research has focused on signal transduction, with an emphasis on both Wnt signaling and circadian rhythms. Early work examined the roles of Protein Phosphatase 2A and Casein Kinase 1 play in these processes. In Singapore, studies of phosphorylation of the PERIOD protein lead to the elucidation of the phosphoswitch model controlling circadian clock speed. In addition, his laboratory collaborated to develop a small molecule inhibitor of Wnt secretion, ETC-159, a drug now in human clinical trials.

Scientific talk: Upstream Regulation of Wnt Signaling: Biology and Therapy

Scientific Speaker

Prof Andrea Maier

- *Oon Chiew Seng Professor in Medicine,*
- *Co-Director of Centre for Healthy Longevity, NUS Medicine*

Andrea Maier (1978), a Fellow of the Royal Australasian College of Physicians (FRACP), graduated in Medicine (MD) 2003 from the University of Lübeck (Germany), was registered 2009 in The Netherlands as Specialist in Internal Medicine-Geriatrics and was appointed Full Professor of Gerontology at Vrije Universiteit Amsterdam (The Netherlands) in 2013. She was the head of Geriatrics at the Vrije Universiteit Medical Center from 2012 to 2016. From 2016 to early 2021 Professor Maier served as Divisional Director of Medicine and Community Care at the Royal Melbourne Hospital, Australia, and as Professor of Medicine and Aged Care at the University of Melbourne, Australia. She continued her career at the National University of Singapore as Co-Director of the Centre for Healthy Longevity.

Professor Maier's research focuses on unraveling the mechanisms of ageing and age-related diseases. During the last 10 years she has conducted multiple international observational cohort studies and intervention trials and has published more than 350 peer-reviewed articles, achieving an H index of 63, spearheading the significant contributions of her highly acclaimed innovative, global, multidisciplinary @Age research group. She is a frequent guest on radio and television programs to disseminate aging research and an invited member of several international academic and health policy committees, including the WHO. She is the President of The Australian and New Zealand Society for Sarcopenia and Frailty Research and serves as selected Member of The Royal Holland Society of Sciences and Humanities.

Scientific talk: Longevity Medicine: The Path towards Prevention

Scientific Speaker

Dr Chris Sham

- *Assistant Professor, Department of Microbiology and Immunology, NUS Medicine*

Dr (Chris) Sham Lok-To is an Assistant Professor in the Infectious Diseases Translational Research Programme (ID TRP) and the Department of Microbiology and Immunology at the National University of Singapore. He trained with Professor Malcolm Winkler at Indiana University Bloomington where he uncovered an ABC transporter-like complex FtsEX in *Streptococcus pneumoniae* that links cell division and cell wall hydrolysis. This complex is widely conserved in bacteria and is crucial for avoiding devastating cell wall lesions during cytokinesis. He then joined the laboratory of Thomas Bernhardt at Harvard Medical School for his postdoctoral training. There, he developed a flippase assay to demonstrate that MurJ is the long-sought cell wall transporter in bacteria. In 2017, Chris started his own research group aiming to understand how the bacterial cell envelope is built as well as how surface polysaccharides facilitate host-pathogen interaction. His work promises to inform vaccine development to combat the rising problem of antibiotic resistance. Chris is the awardee of the American Heart Association postdoctoral fellowship and the National Research Foundation Fellowship, Class of 2019. He also serves as the elected vice president of the Singapore Society of Microbiology and Biotechnology and the Deputy Research Director of the ID TRP.

Scientific talk: Genetic Glycoengineering in Bacteria

Meet Our Career Mentors!

Ace Your Research in Academia

Synopsis: Are you struggling to decide whether a career in academia or industry is the right fit for you? In this panel discussion, we invite professors from NUS Medicine to share with us why academic research is important to drive scientific innovation and the key differences between working in academia and industry.

Prof Wee Joo Chng
Vice-Dean (Research),
NUS Medicine

A/Prof Zhi Xiong Chen
Assistant Dean (Education),
NUS Medicine

A/Prof Kevin Tan
Head, Department of Microbiology & Immunology
Vice-Dean (Graduate Studies),
NUS Medicine

Break into the Fast-tracked Biomedical Industry

Synopsis: The establishment of new R&D for prevention to cure is of prime significance to the scientific community. This session will enlighten us from the industry liaison office of NUS and professionals from the Singapore biomedical industry to help guide and support your career aspiration as an entrepreneur.

Dr Shu Wen Koh
Director, NUS Industry Liaison Office (ILO)
NUHS

Dr William Tan
Associate Director Medical Affairs,
MiRXES

Ms Ashley Wittorf
APAC Head of Business Development
(MedTech), Johnson & Johnson

Dr Sashi Kesavapany
Director, Biomedical Science,
SGInnovate

From Lab Bench to Store Shelves

Synopsis: Looking forward to turning your scientific discoveries into commercially viable products? In this panel discussion, we invite experts with years of experience in translational research to share their views on how scientists bring their innovations to market.

Prof Lawrence Khek-Yu Ho
Director,
Centre for Innovation in Healthcare,
NUHS

Dr Siang Lin Yeow
Head (Enterprise)
National Health Innovation Centre
Singapore (NHIC)

Dr Ajith Isaac
Investment Manager
STRIVE, Pre-Seed and Seed stage enablers

Dr Pei She Loh
Ex-Chairperson, ABSC Congress 2021
R&D Consultant, AVECRIS

Unlock Your Leadership Potential

Synopsis: Our graduate education represents the beginning of being a scientific leader. With our strong technical expertise, we have the potential to scale our impact through leadership. In this session, we have exceptional leaders in STEM, who have built high-performing teams. They will be sharing how they achieved greatness from themselves and inspired it in others.

Dr Xian Jun Loh
Executive Director,
Institute of Materials Research
*and Engineering, A*STAR*

Ms Annie Lim
Vice President-Human Resources
Hummingbird Bioscience

Prof Roger Foo
Zayed bin Sultan Al Nahyan
Professor in Medicine, NUS Medicine

Dr Juliana Chan
CEO, Wildtype Media Group

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Oral Presentation No. 1

Genome-wide CRISPR Screen Identifies an NF2-adherens Junction Mechanistic Dependency for Cardiac Lineage

Lee CJM.[1,2], Autio MI.[1,2], Zheng WH[1,2], Song Y[3,5], Wang SC[3,5], Wong CP[3,4], Chock WK[1], Low BC[3,4,7], Sudol M[6], Foo R[1,2]

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Keywords: Stem-cell differentiation, CRISPR, NF2, Cardiomyocyte development

Cardiac differentiation involves a stepwise clearance of repressors and fate-restricting regulators through the modulation of BMP/Wnt-signaling pathways. However, the mechanisms and how regulatory roadblocks are removed with specific developmental signaling pathways remain unclear. Here, we performed a genome-wide CRISPR screen to uncover essential regulators of cardiomyocyte specification in human embryonic stem cells (hESCs) to better delineate the molecular events that control the earliest step of cardiovascular specification. We identified *NF2*, a Moesin-Ezrin-Radixin Like (MERLIN) Tumor Suppressor, as an upstream driver of cardiomyocyte specification. Transcriptional regulation and trajectory inference from *NF2*-null cells reveal the loss of cardiomyocyte identity and the acquisition of non-mesodermal identity. Sustained elevation of early mesoderm lineage repressor *SOX2* and upregulation of late anti-cardiac regulators *CDX2*, *MSX1* in *NF2* knockout cells reflect a necessary role for *NF2* in removing regulatory roadblocks. Since YAP is a known repressor of mesendoderm genes, we found that NF2 and AMOT cooperatively bind to YAP during mesendoderm formation, thereby preventing YAP activation. Interestingly, YAP activation in *NF2*-null cells is independent of LATS1/2 kinase activity. Mechanistically, cardiomyocyte lineage identity was rescued by wild-type and *NF2* Serine-518 phospho-mutants, but not *NF2* FERM-domain blue-box mutants, showing that the critical FERM domain-dependent formation of the AMOT-NF2-YAP scaffold complex at the adherens junction is required for mesodermal lineage specification. These results provide mechanistic insight into the essential role of NF2 for cardiomyocyte lineage specification by sequestering the repressive effect of YAP and relieving regulatory roadblocks *en route* to cardiomyocytes.

ID#18

Oral Presentation No. 2

Identification of Causal Non-coding Genetic Variants Linked to Cardiac Function

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Keywords: genetic variant, transcriptional enhancer, cardiac function

Genome-wide association studies (GWASs) have discovered a large number of single nucleotide polymorphisms (SNPs) linked to complex traits including cardiac function. However, which of these reported SNPs functionally contribute to the alteration of the phenotype remains a challenging question to answer, especially for those outside protein-coding genes. As many genomic regions harboring the non-coding SNPs exhibit signatures of transcriptional enhancers such as DNase hypersensitivity, and besides malfunctions of enhancers have been observed in cardiac conditions, one common assumption is that non-coding SNPs influence gene expression via changing the activity of corresponding enhancers. Therefore, this study aimed to identify such causal SNPs in cardiomyocytes and decipher the mechanism of their action. First, a list of over 16,000 candidate SNPs was compiled from two previous meta-analysis of GWAS on cardiac function. Next, a support vector machine based on gapped k-mers (gkm-SVM) was trained on datasets of cardiac enhancer sequences, so as to rank the SNPs by the possibility of them affecting the enhancer activity. Based on this prediction, 90 SNPs that topped the list were included in the massively parallel reporter assay (MPRA), which enabled the assessment of enhancer activities for the genomic sequences bearing both alleles of each SNP. From the experiment, we identified 56 SNPs (adjusted $p < 0.05$) that showed significantly different enhancer activities between the reference and alternative allele. Many of these SNPs overlapped with the binding sites of transcription factors known to be essential for cardiac function such as GATA4, GATA6 and PITX2; some also resided within expression quantitative trait loci (eQTLs) in heart tissue. While further validation is required to confirm the allelic effects of these SNPs, this combination of computational and experimental approaches has revealed its potential to empower and accelerate the discovery of causal non-coding SNPs for complex diseases.

ID#13

Oral Presentation No. 3

A balancing Act of the RNA Editing Enzyme ADAR1 in the Liver: Immune Sensing and Suppression

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Keywords: ADAR1, Innate immunity, liver, HCC, self-tolerance, hepatocyte, macrophage, PGRN, EGFR, nucleic acids

Objectives: It is thought that ADAR1-mediated adenosine to inosine (A-to-I) RNA editing and destabilization of endogenous double-stranded RNA (dsRNA) structures normally establishes self-tolerance and prevents their recognition by the immune system primarily through the MDA5-MAVS pathway. Previous studies suggest the concurrent deletion of *Ifih1* gene (encoding MDA5) fully rescues the embryonic lethality following *Adar1* deletion in mice. However, the role and mechanism of action of ADAR1 and RNA editing in innate immunity remains poorly studied. We aim to elucidate the interplay between *Adar1* KO hepatocytes and the hepatic microenvironment to study loss of self-tolerance.
Materials and Methods: In this study, we knocked out *Ifih1* in a liver specific *Adar1* knockout (KO) murine model and found the deletion of *Ifih1* was unable to rescue hepatic damage induced by *Adar1* KO. By performing single-cell RNA-sequencing (scRNA-seq) and spatial transcriptomics, we study the crosstalk between *Ifih1; Adar1* KO hepatocytes and macrophages to study their role in innate immunity.
Results: We observed the persistent activation of interferon (IFN) signalling in *the Ifih1; Adar1* double KO (dKO) hepatocytes intrinsically; and extrinsically, the infiltration of immune cells such as macrophages and CD3+ T cells into the dKO livers. Mechanistically, we showed that dKO hepatocytes highly express *Grn* to recruit *Egfr*-expressing macrophages into the diseased liver. Notably, the *Grn-Egfr* crosstalk pathway and the consequent IFN responses were dramatically repressed in tumors of hepatocellular carcinoma (HCC) patients, providing mechanistic evidence that pre-neoplastic or neoplastic cells, when ADAR1 is overexpressed, may hijack ADAR1-dependent immune tolerance mechanism to facilitate immune evasion.
Conclusions: We have identified that during ADAR1 depletion, other mechanisms besides MDA5-MAVS sensing of self-dsRNA exist to perpetuate nucleic acid induced innate immunity during loss of self-tolerance. Hepatocyte derived *Grn* was found to recruit *Egfr*-expressing macrophages in inflamed mice livers, a crosstalk mechanism suppressed in immunosuppressed HCC.

ID#44

Oral Presentation No. 4

GSTT2 and the Response to BCG Immunotherapy

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Keywords: Bladder Cancer, BCG, GSTT2

Whilst M. bovis Bacillus Calmette-Guérin (BCG) therapy remains the gold-standard for treatment of high-risk non-muscle invasive bladder cancer, 30-40% of patients fail therapy resulting in disease recurrence and progression, which leads to consistently high economic burden. A better understanding of the underlying mechanisms of BCG therapy can aid in elucidating key response pathways which may lead to the discovery of new targets and in turn new approaches. Loss of GSTT2 expression has been associated with modulation of intracellular ROS and BCG survival in bladder cancer cell lines. Additionally, retrospective analysis of bladder cancer patients showed that patients with the GSTT2B deletion responded better to fewer instillations of BCG (6 doses). Thus, a loss of GSTT2 may influence downstream response to BCG. Stimulation of peripheral immune cells from healthy donors and bladder cancer patients revealed that immune cells from GSTT2 negative subjects responded more strongly to BCG stimulation. Loss of GSTT2 expression also conferred stronger immune response to TLR agonists, observed in-vitro in murine splenocytes from WT and GSTT2-KO mice. In-vivo studies in mice revealed differences in the response to BCG therapy, whereby tumors from female BCG-treated KO mice presented with lower expression of immune exhaustion phenotype characterized by lower expression of PD-L1 and CTLA-4. Additionally, tumors from male BCG-treated KO mice were found to have higher T-cell infiltration. Thus, GSTT2 may be able to modulate responses downstream of key immune signalling pathways, which in-turn affect immune activation and response. GSTT2 may also, through direct interaction with intracellular proteins, lipids or nucleotides, to elicit its' immune modulation capacity. Further understanding of the role of GSTT2 in modulating the response to BCG therapy may not only allow GSTT2 to serve as a potential biomarker and tool for patient management but also aid in identifying new targets in the treatment of bladder cancer.

ID#23

Oral Presentation No. 5

Investigating the Role of Rab11a During Enterovirus 71 Infection

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Keywords: Enterovirus 71 (EV71); Hand, Foot and Mouth Disease (HFMD); Neuropathogenesis; Rab11

Enterovirus 71 (EV-A71) causes Hand, Foot and Mouth Disease (HFMD) in children and has been associated with neurological complications. Through a siRNA screen in murine motor neuron-like NSC34 cells, Rab11a was identified as a pro-viral host factor. The family of Rab11 proteins are small GTPases involved in the recycling endosomal pathway and have been shown to be exploited by a number of viruses during infection. Consistently, we showed that in human Rhabdomyosarcoma RD and neuroblastoma SH-SY5Y cells, co-knockdown of both Rab11a and Rab11b GTPAses resulted in significant EV71 viral titer reduction. Using an entry bypass approach and replicon constructs, we showed that Rab11a/b proteins are neither involved in the entry/uncoating of the virus particles, nor in the viral protein translation and viral RNA replication. Instead, a significant reduction in the structural proteins VP2:VP0 ratio was observed in cells treated with Rab11a/b siRNA, suggesting that Rab11 proteins play a role in the maturation of newly formed viral particles by modulating directly or indirectly VP4 cleavage into VP0 and VP2. Confocal imaging, pulldown experiments and proximity ligation assay supported that Rab11 proteins interact with many viral components, including dsRNA intermediate of replication, structural and non-structural proteins. We thus hypothesize that EV71 may highjack Rab11 proteins to bring the relevant viral components together during virus morphogenesis. Consistently, confocal imaging suggested extensive intracellular redistribution of Rab11 proteins during infection. While previous literature has reported a possible role of Rab11 in cholesterol shuttling to EV71 replication complexes, our work has uncovered another role for these proteins during EV71 infection cycle.

ID#38

Oral Presentation No. 6

Red Blood Cell-derived Extracellular Vesicles Display Endogenous Anti-viral Properties and Serve as Effective Oligonucleotide Carriers For SARS CoV-2 Therapy

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Keywords: COVID-19, extracellular vesicles, virus, RNAi, anti-sense oligonucleotide

Objectives: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused the largest pandemic in recent history. Despite the success of vaccines, there still remains no widely accessible treatment that can efficiently suppress the viral infection. RNA-based anti-viral therapies present a promising avenue for the develop of therapeutics, but have yet to reach the safety and efficiency levels required for clinical translation. We have previously shown that red blood cell-derived extracellular vesicles (RBCEVs) are a safe, efficient, and scalable platform for RNA delivery. We aim to design anti-sense oligonucleotides (ASOs) against key SARS-CoV-2 genes and load them into RBCEVs for efficient delivery to lung epithelial cells for the suppression of viral infection.

Materials and Methods: RBCEVs were isolated using pre-established protocols in a workflow consisting of differential centrifugation, filtration, density centrifugation and size exclusion chromatography. RBCEVs were loaded with ASOs targeting conserved regions of key SARS-CoV-2 genes and assayed for the ability to suppress pseudotyped and authentic SARS-CoV-2 infection using plaque reduction neutralization tests, RT-qPCR and immunofluorescent imaging.

Results: RBCEVs exhibited consistent endogenous anti-viral effects against authentic and pseudotyped SARS-CoV-2, inhibiting TIM-1 mediated viral entry in a dose-dependent manner. Upon ASO-loading, RBCEVs were shown to be capable of efficiently delivering ASOs into cells, inhibiting authentic SARS-CoV-2 replication. Intratracheal administration of ASO-loaded RBCEVs to K18-ACE2 mice infected with SARS-CoV-2 resulted in suppression of viral infection, improved treatment outcomes and enhanced survival.

Conclusion: ASO-loaded RBCEVs present a potent and effective therapeutic against SARS-CoV-2. The endogenous anti-viral properties of RBCEVs suppresses viral entry while the ASOs delivered into cells inhibits viral replication, which in combination serves to effectively suppress SARS-CoV-2 infection.

ID#17

Oral Presentation No. 7

Role of CD151 in Influenza-induced Asthma Exacerbation (IAE)

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Keywords: Asthma exacerbation, influenza, CD151

Influenza infection can trigger asthma attacks and a worsening of asthma symptoms that can be fatal. Treatment options for influenza-induced asthma exacerbations (IAE) are suboptimal, suggesting that additional pathways may play a role. We previously showed that CD151, a tetraspanin, positively correlates with asthma severity and enhanced airways hyperresponsiveness (AHR). In separate studies, we showed that CD151 is a host factor of nuclear export signaling in influenza virus infection. Given the crucial role of CD151 in both asthma and influenza infection, we hypothesize that CD151 contributes to IAE. We, therefore, aim to characterize the role and function of CD151 in IAE *in vitro, ex vivo,* and *in vivo*. An IAE mouse model was established by challenging age-matched wild-type -WT C57BL/6 versus CD151-null mice with a clinically relevant allergen, house dust mite (HDM, 25ug), followed by infection with influenza H1N1 virus (15 PFU). The degree of AHR (a marker of IAE), and lung injury were then assessed three days post infection. IAE-treated WT mice showed enhancement in AHR, while CD151-null mice were refractory to such an effect. Interestingly, combined HDM and influenza viral infection enhanced CD151 protein abundance, compared to either allergen or virus infection alone, supporting a more significant role of CD151 in IAE. Lung damage was also more prominent in IAE-treated mice than in allergen- or virus-treated WT mice. In support, precision-cut mouse lung slices (PCLS) from IAE-treated WT mice contracted more compared to lung slices from untreated WT or CD151-null mice. Using *in vitro*, *ex vivo,* and *in vivo* models of IAE, our study unveils heretofore unappreciated mechanisms controlling IAE that are CD151-dependent. A greater understanding of CD151-mediated IAE signaling may lead to the development of novel therapies for IAE, whose treatment options are currently suboptimal.

ID#35

Oral Presentation No. 8

Narciclasine Promotes Lipolysis and White Fat Browning in Diet-induced Obese Mice

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Keywords: Narciclasine, lipolysis, thermogenesis, white fat browning, diet-induced obesity

The imbalance between hydrolysis and synthesis of fat, leading to an excessive expansion of adipose tissue, is one of the major contributors in the development of obesity. Reducing white adipose tissue (WAT) adiposity thus represents an attractive therapeutic strategy for the treatment of obesity. This can be achieved by promoting WAT lipolysis as well as the heat-dissipating process known as thermogenesis. Previously, we demonstrated that the antitumor and anti-inflammatory natural compound, narciclasine (ncls), ameliorates diet-induced obesity (DIO) by enhancing oxidative metabolism in skeletal muscles, reducing fat accumulation, and increasing the mRNA expression of the rate-limiting lipolytic enzyme, *Atgl*, in muscles and adipose tissues of DIO mice. Herein, we provide mechanistic evidence for the lipolytic and thermogenic role of ncls in WAT through *in vitro*, *ex vivo* and *in vivo* models. Stimulation of lipolysis in ncls-treated mature white adipocytes and WAT explants of C57BL/6J mice, as well as chronic treatment of ncls in DIO mice upregulate free fatty acids (FFAs) and glycerol release, as a result of triacylglycerol hydrolysis in lipid droplets. Further transcriptomic analyses validate the role of ncls in lipid catabolism *in vitro* and Western blot analyses reveal that ncls regulates the expression and phosphorylation of key lipolytic enzymes in white adipocytes and WATs through the cAMP-PKA signalling pathway. Additionally, ncls-stimulated lipolysis potentiates subcutaneous WAT (subWAT) browning in mice upon chronic cold exposure. This is corroborated by an elevation of core body temperature, along with increased mRNA expression of brown markers and protein expression of the major thermogenic marker, UCP1. Intriguingly, in parallel with UCP1-mediated thermogenesis, ncls also enhances thermogenesis through a noncanonical mechanism by inducing the transcription of the constitutively active *Gpr3* receptor. Taken together, our findings reveal a working model for the effects of ncls at the whole body and molecular levels.

ID#11

Oral Presentation No. 9

Predicting Individual Brain Regional Atrophy Progression and Cognitive Decline Using Functional Connectome

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Keywords: Alzheimer's disease, disease progression, MRI, machine learning

The network-based neurodegeneration hypothesis posits that neurodegeneration of Alzheimer's disease (AD) targets specific large-scale neuronal network, which mirrors the default mode functional network in health. Our previous work has demonstrated the potential of brain functional connectome in predicting regional atrophy in neurodegenerative disorders. Brown et al. added further evidence at the individual-level by predicting frontotemporal lobar degeneration using a generalized additive model. Yet, no individual nodal atrophy progression prediction model has been developed in AD. Little is known about the possible differential contribution of intra-network and inter-network connectivity to downstream neurodegeneration. Further, existing methods mostly rely on nodal graph theoretical measures which provide a restricted view of functional connectome. Here, we developed an efficient and interpretable individualized, longitudinal nodal atrophy prediction model in the AD spectrum, leveraging the comprehensive graph structure and properties of the brain functional connectome. Our model significantly outperformed benchmark models ($R = 0.46 \pm 0.05$). We identified important FC features that contributed most to network-level atrophy prediction using GNNExplainer. We found that 1) atrophy was most strongly predicted by FC of its own network, followed by hippocampus, default, and control networks; and 2) AD pathology altered how network FC, mainly in hippocampus and higher-order networks, influences future atrophy. Next, we showed that our model predicted cognitive decline (mini-mental state examination (MMSE), clinical dementia rating sum of boxes (CDR-SB)) with high accuracy (MMSE: $R = 0.71 \pm 0.04$, CDR-SB: $R = 0.66 \pm 0.09$). Lastly, the prediction and interpretation results were also validated in an independent Singapore dataset, suggesting the generalizability and validity of our study. In addition to providing evidence for network-based degeneration in AD, the findings represent a key step along the path toward developing prognostic assays for disease progression prediction.

ID#26

Oral Presentation No. 10

Low Plasma Ergothioneine Levels are Associated with Neurodegeneration and Cerebrovascular Disease in Dementia

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Keywords: Dementia, Biomarkers, Cerebrovascular diseases, Ergothioneine, Neurodegeneration

Ergothioneine (ET) is a dietary amino-thione with strong antioxidant and cytoprotective properties and has possible therapeutic potential for neurodegenerative and vascular diseases. Decreased blood concentrations of ET have been found in patients with mild cognitive impairment, but its status in neurodegenerative and vascular dementias is currently unclear. To address this, a cross-sectional study was conducted on 496 community-based participants, consisting of 88 with no cognitive impairment (NCI), 201 with cognitive impairment, no dementia (CIND) as well as 207 with dementia, of whom 160 have Alzheimer's Disease (AD) and 47 have vascular dementia (1). All subjects underwent blood-draw, neuropsychological assessments, as well as neuroimaging assessments of cerebrovascular diseases (CeVD) and brain atrophy. Plasma ET as well as its metabolite L-hercynine were measured using high sensitivity liquid chromatography tandem-mass spectrometry (LC-MS/MS). Plasma ET concentrations were lowest in dementia ($p<0.001$ vs. NCI and CIND), with intermediate levels in CIND ($p<0.001$ vs. NCI). A significant increase in L-hercynine to ET ratio was also observed in dementia ($p<0.01$ vs. NCI). In multivariate models adjusted for demographic and vascular risk factors, lower levels of ET were significantly associated with dementia both with or without CeVD, while ET associations with CIND were significant only in the presence of CeVD. Furthermore, lower ET levels were also associated with white matter hyperintensities and brain atrophy markers (reduced global cortical thickness and hippocampal volumes). The incremental decreases in ET levels along the CIND-dementia clinical continuum suggest that low levels of ET are associated with disease severity and could be a potential biomarker for cognitive impairment. Deficiency of ET may contribute towards neurodegeneration- and CeVD-associated cognitive impairments, possibly via the exacerbation of oxidative stress in these conditions.

ID#10

Lightning Talks Abstracts

Lightning Talk No. 1

Elucidating the Role of ADAR1 in Regulating Immunotherapeutic Response in Multiple Myeloma

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Keywords: Multiple Myeloma, ADAR1, Immunotherapy

Background: Immunotherapies are used as the current standard of care in multiple myeloma (MM). However, MM remains largely incurable with drug resistance and eventual relapse. Adenosine-to-inosine RNA editing, a post-transcriptional modification of dsRNA catalysed by ADAR1 has shown biological and clinical relevance in MM. Importantly, ADAR1 has been demonstrated to be critical in the regulation of innate immune response via the dsRNA sensing pathway. Nevertheless, how aberrant editing associated with dysregulation of immune sensing pathway and its role in regulating immunotherapeutic responses in MM remain largely unexplored. In this study, we elucidated ADAR1's role in mediating responses to lenalidomide—one of the first line immunotherapies used in MM.

Methods: We generated isogenic MM models with differential ADAR1 expression and evaluated its effect on their responsiveness to lenalidomide and its regulation on the dsRNA-sensing pathways. We also established isogenic lenalidomide-resistant (LenaR) cells for validation of ADAR1 and dsRNA-sensor's role in treatment resistance.

Results: We observed that LenaR cells had enhanced ADAR1 expression with a consequential increase in RNA editing, resulting in the impediment of dsRNAs accumulation and suppression of dsRNA-mediated IFN signalling. Accordingly, cells with ADAR1 knockdown demonstrated enhanced sensitivity to lenalidomide and this was associated with dsRNAs accumulation, activation of the dsRNA-sensing pathways and increased inflammatory IFN responses. In concordance, analyses on myeloma patients who underwent immunomodulatory drug (IMiD) – based regimens revealed that dsRNA sensors expression is correlated with clinical outcomes in patients with differential ADAR1 expression. Importantly, we identified that the MDA5 dsRNA-sensing pathway stimulates immunogenicity of MM cells, with ADAR1 being the potential regulating factor contributing to the lenalidomide responsiveness.

Conclusion: Our study identified ADAR1-mediated activation of dsRNA sensing pathway as a novel mechanism regulating lenalidomide sensitivity. The potential role of ADAR1 in modulating immunotherapeutic responses may help unravel potential resistance mechanisms and identify novel therapeutic strategies.

ID#33

Lightning Talk No. 2

Androgen-dependent Tissue Factor Pathway Inhibitor-regulating Protein (ADTRP) Regulates Adipogenesis, Glucose Metabolism and Inflammation Associated with Obesity and Diabetes

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Keywords: ADTRP, adipogenesis, glucose metabolism, inflammation

Obesity and diabetes are leading causes of morbidity and mortality worldwide. Androgen-dependent tissue factor pathway inhibitor-regulating protein (ADTRP) is a recently discovered enzyme that breaks down anti-diabetic and anti-inflammatory fatty acid esters of hydroxy fatty acids (FAHFAs) in adipose tissues. However, the direct effects of ADTRP on glucose metabolism and inflammation underlying the development of obesity and diabetes is unknown. In this study, we aimed to investigate the role of ADTRP in adipogenesis, glucose metabolism and inflammation. We first examined the gene expression of ADTRP during adipogenesis and the effect of ADTRP knockdown using small interfering RNA (siRNA) on adipogenesis in human and mouse 3T3-L1 pre-adipocytes. ADTRP expression was found to be increased during adipogenesis. ADTRP knockdown in the pre-adipocytes reduced expression of adipogenic genes such as adiponectin, C/EBPα, PPAR-γ, FABP4 and GLUT4, and decreased lipid accumulation during adipogenesis, indicating that inhibition of ADTRP prevents adipogenesis. To investigate the effect of ADTRP on glucose metabolism and inflammation, mouse 3T3-L1 mature adipocytes were either treated with ADTRP siRNA or ADTRP plasmid, and glucose uptake and cytokine gene expression were measured. ADTRP knockdown did not affect glucose uptake, but reduced pro-inflammatory IL-6 gene expression in adipocytes. In contrast, overexpression of ADTRP decreased glucose uptake and increased IL-6 and MCP-1 gene expression. These findings suggest that ADTRP can regulate glucose uptake, and may exhibit pro-inflammatory properties in adipocytes. In conclusion, our study provides evidence that ADTRP may play a role in adipogenesis, glucose metabolism and inflammation associated with the development of obesity and diabetes, and can be a therapeutic target for these metabolic diseases.

ID#15

Lightning Talk No. 3

A Concerted Increase in Intron Retention and Readthrough Drives Transposon Expression During Aging and Senescence

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Keywords: aging, senescence, read-through, transposons, intron retention

Transcription of mRNA is a complex process involving several key steps starting with initiation over elongation to termination and co-transcriptional splicing. A breakdown in the fidelity of any of these steps could explain the pervasive and age-dependent expression of genetic elements that lack a functional promoter such as transposons. Based on the genomic localization of these elements we defined intronic, intragenic, gene-proximal and intergenic transposons, since their expression could correspond to different transcriptional defects. Using public RNA-seq datasets from aged human fibroblasts, induced senescence in human cells and RNA-seq from mouse models of aging, we investigated expression of these transposon subgroups. Surprisingly, we found increased age-related transcription of all subgroups that was most pronounced in the human rather than mouse datasets. Expression of intronic transposons was correlated with age-related intron retention, whereas expression of gene-proximal transposons correlated with transcriptional read-through, a transcriptional deficit that also increased with age. There was no consistent change in read-in transcription with aging. Finally, there was a marked shift for differentially expressed transposons to be located in genes that show age-related upregulation, although the few intergenic transposons that were expressed also increased with age. We show that transposon expression is likely a marker of increased intron and readthrough transcription which may have implications on which of these phenomena we should target in order to slow age-related diseases. Finally, our work provides hints as to the optimal biomarkers of aging.

ID#20

Lightning Talk No. 4

Making Bioprinting One-step Closer to Translational Application – Capillary Vessel Printing by Interfacial Polyelectrolyte Complexation

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Keywords: Bioprinting, Vasculature, Polyelectrolyte Complexation

Three-Dimensional (3D) printing, which is also known as additive manufacturing, is a very precise fabrication technology produces customized constructs via a layer-by-layer fashion. This technology suits very well for biomedical applications as the spatial features of many biological systems are highly specific and often vary across individuals. It is believed that 3D printing will be the solution for challenges in various healthcare sectors such as regenerative medicine, drug discovery/developments, diseases modelling, high throughput screening and bio-hybrid robotics. To date, 3D-printing of acellular constructs has achieved considerable translational success as seen in quite several FDA-approved applications. On the other hand, the 3D printing involving living cellular constructs, which is also known as bioprinting, has encountered a number of challenges. Among all, one major challenge is the lack of an efficient technique for establishing and integrating physiological vasculature network into a bioprinted tissue. Because of this, the bioprinted cellular constructs often show poor viability and functionality. In our lab, by using polyelectrolyte interfacial complexation phenomena, a technique suitable for the bioprinting of tubular constructs was established. Oppositely charged polyelectrolyte solutions were placed co-centrically in a coaxial nozzle. Upon printing, the extruded polyelectrolytes met and immediately complexed into tubular constructs in designated patterns. With the vascular cells imbedded, the in-situ formed tubes function as cell attachment and proliferation substrate, which eventually made the printed cellular construct resemble the anatomy of capillary blood vessels. This technology will be beneficial for a wide range of bioprinting-related downstream applications such as tissue vascularization and organ chip fabrication.

ID#45

Lightning Talk No. 5

The Impact of Yo-yo Dieting on Cardiac Health

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Keywords: Cardio-metabolic disease, cardiac health, high-caloric diet, yo-yo dieting, weight cycling

Intentional body weight loss and regain that is caused by "yo-yo" dieting is a population phenomenon among women and men, the young and the old in the modern society. Clinical data suggests that sustained fluctuations in energy balance during weight cycling can impact cardiovascular risk factors, including blood pressure, heart rate, cardiac workload, sympathetic activity, blood glucose and lipids. However, association with cardiovascular morbidity and mortality is debated. Furthermore, mechanisms underlying the effects of weight cycling on cardiac health outcomes have not been previously explored. Here, we aimed to investigate how repeated yo-yo dieting impacts cardiac health focusing on how alterations between standard and high-caloric diet affect cardiac metabolic profiles through transcriptomic analysis together with metabolic parameters (such as blood pressure, plasma lipids, blood glucose), measured longitudinally using a rodent model. By far, our findings reveal that despite the overall normalization of metabolic parameters, mice going through yo-yo dieting exhibit a more cardiac disease-related phenotype, even when comparing to chronically high caloric diet- fed mice.

ID#8

Lightning Talk No. 6

The Role of Long Non-coding RNA *VENTHEART* in Cardiomyocyte Differentiation and Maturation

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Keywords: single cell RNAseq, stem cell derived cardiomyocytes, long non-coding RNA, ventricular cardiomyocyote, action potential

Cardiac development is a crucial and highly coordinated process regulated by transcriptional, translational and epigenetic modulators. While genetic pathways during early stage of committing to cardiac cell fate have been extensively studied and relatively well-defined, regulation for subsequent cardiac lineage specification, terminal differentiation and maturation is less well-understood. Long coding RNAs (lncRNAs) have been shown to play a role in controlling cardiac gene expression during heart development and diseases. To identify lncRNAs in cardiac development more relevant to human, we used human pluripotent stem cell derived cardiomyocytes (hPSC-CMs) as an *in vitro* cell model for cardiac differentiation and development. Through single-cell RNAseq analysis of maturing hPSC-CM in prolonged culture, we identified a novel lncRNA *VENTHEART* (*VHRT*), which was highly co-regulated with cardiac development and ventricular-specific genes including *MYL2* and *MYH7*. *VHRT* deletion lead to disruption of cardiac gene expression profile and sarcomeric organization in both human embryonic stem cell (hESC) and human induced pluripotent stem cell (hiPSC) derived cardiomyocytes with mostly ventricular population. Interestingly, similar disruption was not observed when cells with *VHRT* deletion were differentiated toward an atrial-specific lineage, indicating the subtype-specific effect of *VHRT*. In addition, *VHRT* deletion lead to prolonged action potential duration in ventricular-like but not atrial-like cardiomyocytes. These findings provide evidence for the identification of the long non-coding RNA *VHRT* in ventricular CM maturation and function.

ID#29


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Poster Presentation Abstracts

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3	Yeap Hui Wen	Macrophage Cell Death as an Antimicrobial Mechanism Against Extracellular Bacterial Infection
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S/L	Name	Abstract Title
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Poster Presentation No. 1

A Human Monoclonal Antibody Isolated from the Iga Repertoire of a Chronically Exposed, Asymptomatic Individual Mediates Protection Against *Mycobacterium Tuberculosis*

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Keywords: Mycobacterium tuberculosis, monoclonal antibodies, TB prophylaxis

Tuberculosis (TB) is a life-threatening airborne infectious disease caused by the intracellular pathogen *Mycobacterium tuberculosis* (Mtb). TB has become a global health concern, with a quarter of the global population being latently infected and 10 million active infections annually. The emergence of multidrug-resistant Mtb has developed into a major setback for current antibiotic treatment regimes. Under these circumstances, better vaccination and/or alternative therapeutic approaches are vital to combat the global disease burden. Whilst a functional role for humoral immunity in Mtb protection remains ambiguous, several studies have shown that antibodies play an important role in host defence against this pathogen. Moreover, the potential of antibody therapy/prophylaxis for combating microbes that are resistant to antibiotics represents an interesting alternative approach for targeting this disease. Studying antibody repertoires and identifying natural protective antibodies against Mtb from asymptomatic individuals who remain immune to active disease despite being in a high Mtb exposure setting, would also have significant implications for vaccine developmental strategies. Our aim was to develop fully human monoclonal antibodies against whole-cell Mtb from a cohort of asymptomatic TB health care workers and conduct a thorough characterization of the isolated antibodies. We performed IgG and IgA high-throughput screening from the donor memory B cell repertoire using gamma-irradiated whole-cell Mtb as the target antigen. From the IgA/IgG repertoire, we identified a number of human monoclonal antibodies targeting the Mtb surface antigens. A detailed biophysical and biochemical characterization of their specificity, function and fundamental biology has been studied.

ID#1

Poster Presentation No. 2

The Missing Link Between Capsule Synthesis and Cell Division

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Keywords: *Streptococcus pneumoniae*, capsular polysaccharide, bacterial tyrosine kinase, bacterial cell division

The bacterial cell envelope is a complex, multi-layered structure that protects the cell from the environment. In gram-positive bacteria, it consists of a thick peptidoglycan layer decorated with teichoic acid and capsular polysaccharide (CPS). Regulation and coordination of the synthesis of different envelope layers are crucial for survival in host niches. For peptidoglycan, this process is driven by two protein complexes called the divisome and the elongasome. Nevertheless, how CPS synthesis is coordinated with peptidoglycan synthesis remains unclear. In this study, we used pulse-chase experiments and immunofluorescence microscopy to show that CPS synthesis is initiated at the mid-cell in *Streptococcus pneumoniae*. This coordination is dependent on the bacterial tyrosine kinase CpsCD. CpsC localises to the mid-cell and its location is governed by the divisome. Forcing CpsC to the cell pole by PopZ is sufficient to mislocalize the CPS synthesis complex. Next, we sought to determine the protein(s) that recruits CpsC to mid-cell. Deletion of various *cps* genes did not alter CpsC localisation. However, depletion of proteins associated with the divisome (FtsZ, EzrA, FtsI, FtsW, FtsQ), but not the elongasome, resulted in CpsC delocalisation and aberrant capsule synthesis. Together, we propose the CPS complex is part of the divisome that arrives during the final stage of cell division.

ID#2

Poster Presentation No. 3

Macrophage Cell Death as An Antimicrobial Mechanism Against Extracellular Bacterial Infection

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Keywords: apoptosis, necroptosis, NF-κB, macrophage, diarrheagenic bacteria

Macrophages are known to activate programmed cell death including apoptosis, pyroptosis and necroptosis to eliminate the survival and replicative niche of intracellular diarrheagenic bacteria, for example, *Salmonella* Typhimurium and *Shigella flexneri*. Whether macrophages activate cell death to counteract extracellular diarrheagenic bacteria, and how these pathogens subvert host cell death signalling remain poorly understood. To address these questions, we infected bone marrow-derived macrophages with two extracellular pathogens: *Yersinia pseudotuberculosis* and *Citrobacter rodentium* which inject diverse virulence factors known as type 3 secretion system (T3SS) effectors into host cells. While *Y. pseudotuberculosis* and *C. rodentium* T3SS effectors are known to inhibit pro-inflammatory NF-κB signalling, we discovered that macrophages retaliate by activating an unconventional apoptotic pathway as a host defence strategy. We further found that *Y. pseudotuberculosis* and *C. rodentium* effectors differentially regulate NF-κB signalling and expression of anti-apoptotic factors, which modulates macrophage susceptibility to a caspase-8-independent form of cell death - necroptosis. Since necroptosis is poorly described in extracellular diarrheagenic bacterial infection and *C. rodentium* expresses EspL effector to antagonise necroptosis, we discerned the mechanism underpinning macrophage necroptosis. Our preliminary findings demonstrated a role for NF-κB-driven expression of anti-apoptotic factor, cFLIP, in sensitising macrophages to necroptosis during *C. rodentium* Δ*espL* infection. On the other hand, *Y. pseudotuberculosis* T3SS effector efficiently inhibits NF-κB signalling, resulting in low cFLIP expression and apoptosis activation in macrophages. Taken together, this study unraveled macrophage apoptosis and necroptosis as important anti-extracellular pathogens response. Future work elucidating the host-pathogen arms race and the physiological importance of cell death signalling offer exciting insights into gastrointestinal pathologies.

ID#3

Poster Presentation No. 4

Characterization of a Clec9A-targeting Vaccine Strategy Against COVID-19

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Keywords: SARS-CoV-2, Clec9A, Ribosomal Binding Domain, Antibody, T Cell

Current COVID-19 vaccines require repeated boosters to maintain effective protection against infection. Here, we present a novel vaccine candidate, namely Clec9A-RBD, which consists of the genetic fusion between an anti-Clec9A monoclonal antibody and SARS-CoV-2 spike receptor binding domain (RBD). Clec9A-RBD targets conventional type 1 dendritic cells and was found to elicit long-lasting antigen specific humoral and cellular responses upon a single shot. We first showed that a single immunization of Clec9A-RBD induced high RBD-specific antibody titer with a Th1 isotype profile that persisted up to 21-months in mice, and was accompanied with a progressive increase in antibody binding to wild-type and variant RBD (Alpha, Beta, Gamma, Delta and Omicron). Moreover, using a SARS-CoV-2 surrogate virus neutralization test, we observed that immune sera neutralizing activity against wild-type and variants increased over time, which was supported by robust and continual affinity maturation. Furthermore, longitudinal increase in immune sera antibody-dependent cellular cytotoxicity (ADCC) activity was observed against wild-type and variants spike-expressing cells. Finally, restimulation of splenocytes with RBD overlapping peptides demonstrated the induction of a polyfunctional Th1-biased response against wild-type and most variants. Assessment of T-follicular helper (Tfh) cell, long-lived plasma cell, and memory B cell response and persistence, are underway to further characterize the immunological properties of Clec9A-RBD. Collectively, our findings highlight the immunological benefits derived from a Clec9A-targeting vaccine strategy and presents Clec9A-RBD not only as a standalone vaccine approach, but also a potential boosting strategy to enhance the strength and durability of existing COVID-19 vaccines.

ID#4

Poster Presentation No. 5

Urolithin A Promotes Mitochondria Biogenesis and Autophagy and Extends Longevity

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Keywords: Urolithin A, Autophagy, Mitochondria Biogenesis, Aging, Longevity

Objectives: To validate the robustness of Urolithin A as an anti-aging therapeutic. Evidence that Urolithin A is a robust geroprotector is rather weak.

Materials and Methods: HEK293 cells and C2C12 myoblast were used for invitro mitochondria biogenesis and autophagy experiments. A combination of techniques were used including qPCR, Western blot, FACS and Confocal imaging.

Results: We show that Urolithin A upregulated multiple pro-longevity pathways including fatty acid metabolism, autophagy and mitochondria biogenesis. Urolithin A also downregulated the pro-aging pathway; mTOR. Furthermore when tested in an *in vivo* vertebrate model, we show that Urolithin A is able to delay aging. Urolithin A was shown to extend longevity in the African Turquoise killifish. To the best of our knowledge this is the first work showing that Urolithin A can extend longevity in vertebrate model organisms.

Conclusions: Urolithin A shows promise for use for as an anti-aging therapeutic.

ID#5

Poster Presentation No. 6

A Genetic Glycoengineering Platform in Bacteria

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Keywords: *Streptococcus pneumoniae*, glycans, glycosyltransferase, glycoengineering, flippase

Glycans and glycoconjugates are present in all living cells. They constitute one of the four main classes of biomolecules and perform crucial cellular functions. Yet, tools to alter their structure and composition are still lacking. In prokaryotes, surface glycans can be manifested in the form of capsular polysaccharides (CPSs), which are important for evading the host immune system. Most CPSs are synthesized by the activity of glycosyltransferases (GTs) on the cell membrane, and the chemical composition of the final product is largely dependent on the specificity of the GTs involved. Despite their immense importance in biology, tools for investigating GT specificity are mainly limited to biochemical reconstitution. Not only does it require sophisticated analytical methods, but the reconstitution experiment also requires many hard-to-obtain substrates and their derivatives. Consequently, little is known about how GTs produce various glycosidic linkages to connect a diversity of donor and acceptor molecules. Here, we report a genetic glycoengineering approach to modify the capsular polysaccharide in *Streptococcus pneumoniae*. Powered by conditional essentiality of the pathway, cells were reprogrammed to install subtly different glycosidic linkages, as well as to substitute and delete sugar residues. As a proof of principle, we were able to delete the last sugar residue in serotype 2 capsule, resulting in a change in surface charge of the cell, which confirmed the role of the flippase as the quality control checkpoint of the pathway, and isolated glycosyltransferase variants with relaxed specificity. The overall goal of this project is to establish a glycoengineering platform that will allow us to understand the mechanism of GT specificity and assist glycoengineering efforts to generate molecules with desired sugar compositions and linkages.

ID#6

Poster Presentation No. 7

Substrate Specificity of Capsule Flippase in *Streptococcus Pneumoniae*

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Keywords: MOP transporters, *Streptococcus pneumoniae*, capsular polysaccharides, lipid flippase, capsule

MOP (Multidrug/Oligosaccharidyl-lipid/Polysaccharide) family flippases are present in all life forms. They are responsible for transporting lipid-linked precursors across the cell membrane to support the synthesis of various glycoconjugates. While significant progress has been made in elucidating the transport mechanism of the MOP transporters, how these ubiquitous flippases select for their substrates remains unclear. We exploited *Streptococcus pneumoniae* with diverse capsular polysaccharide (CPS) structures to investigate the substrate specificity of the capsule transporters. There are over a hundred known pneumococcal serotypes, each producing a unique capsule. The capsule flippases involved in the synthesis of the CPS are known to be specific, and sequence similarities cannot predict whether they are interchangeable. Here, we developed a high-throughput approach to systematically test nearly 6,000 combinations of cross-complementation among the non-cognate flippases. A directed evolution experiment was also performed to identify gain-of-function flippase variants that flip structurally distinct cargos. The isolated variants could substitute the cell wall peptidoglycan flippase *ytgP* and two other non-cognate CPS flippases. The findings provide insights into the substrate specificity of MOP transporters.

ID#7

Poster Presentation No. 8

Influence of Glycan Structure on Colonization of *Streptococcus Pneumoniae* on Human Respiratory Epithelial Cells

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Keywords: *Streptococcus pneumoniae*, Capsular polysaccharide, Host-pathogen interaction, Human nasal epithelial cells, Human bronchial epithelial cells.

The bacterial glycan capsular polysaccharide (CPS) is a major virulence factor in *Streptococcus pneumoniae* that protects the cell from host immunity. Approximately 100 types of CPS (serotypes) have been identified. Epidemiology studies suggest serotypes influence pneumococcal carriage, which acts as a reservoir for transmission and is a prerequisite for invasive diseases. Nevertheless, how the composition and configuration of CPS affects colonization remain unclear. We constructed 258 isogenic capsule-switch mutants representing 84 serotypes in *S. pneumoniae*. The mutants were chromosomally tagged to allow abundance of each strain to be quantified by amplicon sequencing. To understand interactions between pneumococcal serotypes and the human epithelia, we adopted the primary human nasal and bronchial epithelial cells. The respiratory cells are grown at an air-liquid interface (ALI) and display features similar to the upper and lower airways respectively. The binding of the mutants on primary human nasal and bronchial epithelial cells were measured. Contrary to the paradigm, surface charge did not significantly affect epithelial cell binding. We also elucidated structural features that may affect adhesion to respiratory cells, such as rhamnose residues or human-like glycomotifs. Pneumococcal colonization on nasal epithelial cells also stimulated the production of IL-6, GM-CSF, and MCP-1 in a capsule-dependent manner. Our results establish the importance of CPS structure to colonization and survival on the human airway.

ID#9

Poster Presentation No. 9

Homoarginine is a Novel Predictor of Sepsis Outcomes - A Prospective, Single-centre Observational Study

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Keywords: Homoarginine, Methylarginines, Sepsis, Critical Care, Emergency Medicine.

Objective. This study aims to determine primary metabolic predictors of hospital length of stay, length of ICU stay and sepsis in emergency department (ED) patients.
Methods. The study was conducted in adult patients recruited from the ED who were diagnosed with either sepsis (n=128) or infection (n=255). Twenty-four patients had direct admission to the intensive care unit (ICU). Using targeted LC-MS/MS, a panel of 335 oxidative stress and related markers were profiled for each patient in addition to a set of healthy, age-matched controls (n=82). Clinical outcomes were length of total hospital stay, length of ICU stay and post-hoc, adjudicated sepsis severity scoring.
Results. Using computational biology tool, we identified 3 major metabolites of the nitric oxide (NO) pathway, which returned lysine, glutamine and homoarginine (hArg), all of which were decreased in sepsis when compared with healthy controls ($P<0.001$). ROC curves showed the hArg was superior and discriminated both sepsis from controls (AUC = 0.86 [95% CI 0.81 - 0.91]), and sepsis from infection (AUC = 0.73 [95% CI 0.68-0.78]). The 25th percentile of hArg (odds ratio (OR) = 8.57 [95% CI 1.05-70.06]), was associated with hospital length of stay (LoS) (incidence rate ratio (IRR)=2.54 [95% CI 1.83-3.52]) and ICU length of stay (incidence rate ratio (IRR) = 18.73 [95% CI 4.32-81.27]) respectively. In the prediction of sepsis severity and ICU stay, hArg had superior performance compared with traditional markers of sepsis.
Conclusion. hArg was associated with sepsis severity and clinical outcomes. Our findings suggest hArg as a novel clinical biomarker to identify patients at risk, which could provide effective solution for disposition decision-making and health care cost.

ID#42

Poster Presentation No. 10

Novel Interactions Between a Unicellular Parasite and the Gut-brain Axis

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Keywords: *Blastocystis*, Enterochromaffin Cells, Tryptophan, Indole, Serotonin

Objectives: *Blastocystis* is a unicellular eukaryotic parasite able to infect the human colon. Whether it is pathogenic has been a topic of debate in the scientific community since its discovery. Some evidence links *Blastocystis* infection to improvements in gut health, while other evidence shows a link between the parasite and the common gut disease irritable bowel syndrome (IBS). A paper published by Eme *et. al.* in 2017 showed that *Blastocystis* expresses the prokaryotic gene tryptophanase. In prokaryotes, this gene converts the amino acid tryptophan into the signalling compound, indole. As tryptophan and indole are components of the gut-brain axis and have been associated with IBS, we sought to investigate the function of this prokaryote gene expressed in a eukaryotic organism.
Methods: A GST-tagged *Blastocystis* tryptophanase sequence was transformed into *E. coli.* The expressed protein was purified before being characterized with off-the-shelf tryptophan assay kits. RT-qPCR and ELISA were used to assess serotonin synthesis and associated gene expression in RIN14B cells.
Results: Analysis using PyMOL and NCBI highlighted an ~40 amino-acid long domain absent from known tryptophanase and tryptophanase-like proteins, located on the exterior of the tertiary structure. Assessment of the enzyme's ability to metabolise tryptophan revealed a greater affinity of *Blastocystis* tryptophanase for its reverse reaction: the synthesis of tryptophan from indole. Following this, we showed that *Blastocystis* is not only capable of tryptophan synthesis, but can also influence tryptophan-dependent serotonin synthesis in RIN14B cells, an enterochromaffin cell model.
Conclusions: The unusual domain suggests the enzyme's capacity for unexpected function, borne out by its ability to produce tryptophan. Enterochromaffin cells are responsible for the majority of enteric serotonin synthesis, and the ability of *Blastocystis* to influence this process may affect gut health. IBS has been linked to fluctuations in enteric serotonin, as well as tryptophan and indole.

ID#14

Poster Presentation No. 11

Role of microRNAs in the Regulation of CD151 Expression in Asthma

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Keywords: Asthma, miRNAs, CD151

Asthma is a chronic inflammatory respiratory disease whose treatment options remain suboptimal, suggesting additional pathways may play a role. We previously showed that the expression levels of the tetraspanin CD151 correlated with asthma severity and contribute to airway hyperresponsiveness. However, no studies have explored the molecular mechanisms regulating CD151 expression in asthma. Our preliminary studies showed that CD151 expression is regulated post-transcriptionally; hence we hypothesize that microRNAs (miRNAs) could play a role in regulating CD151 expression in asthma. Candidate miRNAs (miR-22-3p, miR-103a-3p, miR-124-3p, miR-199a-3p and miR-506-3p) were selected based on their ability to target CD151 through *in silico* predictions and/or current literature. These miRNAs were assessed for their ability to bind to CD151 3'UTR, reduce CD151 mRNA levels and CD151 protein levels through luciferase assay, q-PCR, and western blot, respectively. Experiments were performed in airway epithelial (hAEC) and smooth muscle (hASM) cells – cell types that play integral roles in asthma pathophysiology. miRNA profiling was also performed to identify key dysregulated miRNAs in asthma, from *in vitro* and *in vivo* models to clinical samples of asthma patients. The miRNA profiles obtained were analyzed together with existing databases from the literature. Though miR-22-3p, miR-103a-3p, and miR-124-3p target CD151 gene expression in other cell types, only miR-506-3p and miR-199a-3p significantly target CD151 to reduce mRNA and protein levels in hAECs and hASM cells. This finding reveals a cell-type-dependent nature of the regulation of CD151 expression by miRNAs distinct to the asthma phenotype. miRNA profiling obtained from clinical samples supports the complex nature of miRNA involvement in different asthma endotypes. Further characterization studies on the role of miRNAs regulating CD151 expression may yield a greater understanding of asthma pathogenesis and endotypes and, therefore, the development of novel treatment options for asthma, for which there is currently no cure.

ID#16

Poster Presentation No. 12

Possible Viral Interference Leading to Protection from Subsequent Respiratory Viral Infections – Results of an Observational Study at a Singapore Teaching Hospital

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Keywords: respiratory viral infection; viral interference; cross-protection; influenza; adenovirus.

To determine which viruses provide protection against specific subsequent viral infection. We conducted a retrospective review of the hospital epidemiology database of clinical laboratory reports in our 1200-bed teaching hospital. Testing is based on symptomatic patients using primarily the D3 Ultra™ DFA Respiratory Virus Screening and Identification Kit (Diagnostic Hybrids, Inc., USA). In a preliminary analysis of patients who were positive by immunofluorescence assay (IF) from April 2017 to June 2018, we compared the frequency of patients infected with the four main viruses identified by IF in terms of subsequent respiratory viral infections detected by both IF and PCR based assays. Data were compiled and analysed in Microsoft EXCEL and using SPSS. A total of 589 patients were IF positive. The majority were children, with a slight male predominance, 332 (56.4%) vs 257 (43.6%). Comorbidities were present in 176 (29.9%) patients predominantly asthma, 60 (10.2%) and other chronic respiratory diseases, 52 (8.8%). The most common viruses identified during the current study period were RSV, 301 cases (49.4%), Influenza, 195 (32%), Parainfluenza, 62 (10.2%) and Adenovirus, 34 (5.6%) cases. Thirty-six patients had subsequent respiratory viral infections identified up to Jan 2022. These included RSV, (22), Influenza, (14), EV/RV, (11), Parainfluenza, (8) and SARS CoV2 (7) occuring a median of 336 (11-1731) days after the first infection. Patients infected with adenovirus (6.2%), RSV (8.6%) and influenza (4.8%) virus were less likely to be infected with another respiratory virus in the subsequent five-year period than patients infected with parainfluenza virus (17%, OR: 0.41, 95% CI 0.2-0.9, p=0.03). It is possible that prior infection with certain viruses protects individuals against subsequent respiratory viral infections. Larger prospective studies which incorporate host immune responses are needed to better understand if viral interference can explain the epidemiology of various respiratory pathogens over time.

ID#21

Poster Presentation No. 13

Super-enhancer-driven PPP1R15B as an Oncogenic and Potential Therapeutic Target in Multiple Myeloma

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Keywords: multiple myeloma, epigenetics, super enhancer

Objectives: Growing evidence suggests that alterations in epigenetic landscape contribute to pathogenesis of multiple myeloma (MM). MM cells are highly dependent on unfolded protein response signaling pathways due to high level of endoplasmic reticulum stress. Phosphorylation of eIF2α can attenuate protein translation. The PPP1R15B(denoted as R15B hereafter) gene encodes a regulatory subunit of eIF2α-specific phosphatase complex. In this study,we identified super enhancer (SE)-driven oncogenes specific in MM with a particular focus on a candidate gene R15B, whose functional roles in MM remain largely elusive.

Methods: We performed H3K27Ac ChIP-seq on MM cell lines, primary MM patient samples, normal CD138+ plasma cells and memory B cells. ROSE analysis was used to annotate SEs and their associated genes. A combination of public data mining, RNAi, overexpression and CRISPR/Cas9 technologies were conducted to determine the oncogenic effects of R15B in MM. Transcriptome analysis of MM cell line H929 with R15B KD and scrambled control was performed. To further study the interactions between SE and its promoters, we also performed H3K27ac HiChIP.

Results: We have identified R15B as one of the SE-associated genes specific to MM patient samples and cell lines. SE activity was correlated with the expression level of R15B. Higher expression of R15B predicted poor overall survival of MM patients, suggesting its clinical relevance in MM pathogenesis. R15B KD or KO significantly reduced cell viability, clonogenicity and induced G2/M arrest. ChIP-qPCR assays showed that C/EBP-β is strongly enriched at R15B SE region. PPP1R15B promoter-enhancer interactions were confirmed by HiChIP. We also found that salubrinal, a selective inhibitor of eIF2α phosphorylation, inhibited MM cell proliferation in a dose-dependent manner.

Conclusions: Our integrative approaches identified R15B as a novel SE-driven oncogene. We propose that targeting R15B may serve as a new approach for effective anti-myeloma therapy, which warrants further clinical investigation.

ID#32

Poster Presentation No. 14

Prediction of Hepatocellular Carcinoma Based on Exosomal Gene Expression Using Machine Learning Approach

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Keywords: Hepatocellular carcinoma, Exosome, Machine learning, Predictive model

Objectives: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide. Clinically, serum alpha-fetoprotein (AFP) remains the most commonly used serologic screening test for the initial diagnosis of HCC, however it suffers from low levels of sensitivity and specificity. While novel biomarkers that may serve as screening tools have been identified, there is a gap of knowledge in the clinical utility of translating such biomarkers to bedside clinical markers. Therefore the identification and development of biomarkers with clinical applicability to improve the detection of HCC is urgently needed. This paper proposes a Machine learning approach using Exosomal-derived RNAs to distinguish HCC patients from non-HCC individuals and predict if an individual is likely to develop HCC with biological validation from patient tissue data.

Materials: Exosomal gene expression profiles of 35,717 RNAs from 112 HCC patients and 118 healthy samples were obtained from exoRBase database, while expression profiles of 49 patient tissue samples from the National Cancer Centre Singapore (NCCS) were obtained using Microarray.

Methods: Exosomal expression profiles were subjected to pre-processing followed by feature selection using Recursive Feature Elimination with a 5-fold Cross Validation to select for potential predictors. The biological relevance of predictors was validated by patient tissue data through differential expression (DE) analysis.

Results: A 68 gene signature which consists of 2 lncRNAs and 66 mRNAs were identified as potential predictors. These predictors have good predictive performance (AUC: 0.70-0.95, Sensitivity: 0.64-0.94 and Specificity 0.67-0.94). 17 mRNAs from the 68 signatures were differentially expressed ($p<0.05$, $|FC| > 1.5$) in patient tissue samples.

Conclusion: Our 68 gene signature may facilitate the development of non-invasive diagnostic tests for the detection of HCC. Future work includes further downstream analysis to elucidate the pathways involved by potential predictors.

ID#34

Poster Presentation No. 15

Exosome Biogenesis Pathway Play a Significant Role in Survival of Daratumumab Resistant Hematological Malignancies

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Keywords: Hematological malignancies, Daratumumab Resistance, Exosomes

Daratumumab is a human monoclonal antibody that targets cell surface CD38 receptor in hematological malignancies. In our study, we observed that Daratumumab treatment was effective in a subset of Natural Killer/T-cell lymphoma (NKTL) cell lines with CD38 expression. However, recent phase II study have shown that this response in NKTL patients were short-lived. This was also observed in studies that demonstrated high risk of Daratumumab resistance in treated Multiple Myeloma (MM) patients Therefore, in this study, we sought to investigate mechanisms involved in Daratumumab resistance. We generated isogenic cell lines that are either sensitive or resistant to Daratumumab treatment in NKTL as well as MM and T acute lymphoblastic leukemia (T-ALL) to validate our findings. We performed RNA sequencing analysis to compare differential gene expression. We then isolated exosomes and conducted Nanoparticle tracking analysis to assess exosome secretion of the isogenic cell lines. Exosome Biogenesis inhibitors were used to assess effects on resistant cell lines. Coculture experiments were then conducted to evaluate possible effects of exosome uptake by recipient cell lines. We demonstrated that Daratumumab resistant cell lines proliferate at a higher rate, accompanied by an upregulation of proteins involved in exosome biogenesis. Inhibition of these pathways lead to a more pronounced cell death in isogenic cell lines with the resistant phenotype. Addition of exosomes isolated from Resistant cell lines promote enhanced cell viability of Sensitive cell lines and resistance to Daratumumab-induced CDC. Taken together, current findings suggest that exosome mediated pathways may play a key role in contributing to the survival and resistance phenotype of Daratumumab resistant cell lines. The Role of exosomes in Daratumumab resistance has yet to be explored fully. This study may also help identify novel therapeutic strategies to overcome daratumumab resistance in patients.

ID#36

Poster Presentation No. 16

The Role of Glucocorticoids on CD151 Expression in Influenza A Virus Replication

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Keywords: CD151, Glucocorticoids, Influenza A Virus

Objectives: Owing to its potent anti-inflammatory properties, glucocorticoids (GC)s are prescribed for influenza infection-related hyperinflammatory complications, like acute respiratory distress syndrome or pneumonia. However, GC application is highly controversial and associated with heightened disease-related mortality as GCs increase influenza A virus (IAV) titre. GC-induced immunosuppression has been proposed as the underlying mechanism for this increase in viral titre; however, this mechanism is neither well characterised nor understood. Previously, our laboratory showed that tetraspanin, CD151, is a novel host factor of IAV replication. Preliminary studies revealed that GC treatment upregulates CD151 expression in airway epithelial cells. Therefore, we hypothesise that GC-induced increase in IAV replication, IAV titre, and disease-related mortality is mediated by CD151.

Materials and Methods: Using *in vitro* human airway epithelial cells (hAECs), we first validated that CD151 alone can enhance IAV titre. We also determined the effect of GC, fluticasone propionate (FP), on airway resistance in *ex vivo* precision-cut mouse lung slices. Finally, using CD151 CRISPR-knockout hAECs and *in vivo* CD151-null mice infection models, we treated the models with FP and analysed virus titre, protein expression and localisation.

Results: CD151 alone is sufficient to significantly enhance IAV titre, further supporting its essential role in viral replication. FP treatment enhanced CD151 expression both *in vitro* and *in vivo*. Importantly FP-enhanced IAV titre is CD151-mediated since viral titre levels were significantly reduced in CD151-null-infected mice as compared to wild-type-infected mice. We also discovered a novel CD151-mediated pathway where FP upregulates IAV nucleoprotein (NP) expression. NP is essential for viral RNA replication and transcription but also for nuclear transport and packaging of viral particles.

Conclusion: Our study findings suggest a potential novel avenue for optimising GC therapy regimens for hyperinflammation caused by influenza infections; targeting CD151 to hamper IAV replication while preserving the beneficial anti-inflammatory properties of GCs.

ID#37

Poster Presentation No. 17

Glutamine Addiction of cMAF Overexpressing Cells Drives Dysregulation of Purine Metabolism

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Keywords: Multiple myeloma, metabolism, glutamine

c-MAF is an oncogenic bZIP transcription factor, frequently overexpressed in Multiple Myeloma. Patients with t (14 ; 16) c-MAF translocation constitute a high-risk group with adverse outcomes. Since transcription factor mediated phenotypes are not classical drug targets, elucidating pathways downstream or associated with c-MAF could present as potential therapeutic targets. Critically, studies showed a class of recurrently deregulated metabolic genes in c-MAF signatures broadly classified with underexplored roles in MM. Hence, this warrants further studies to gain deeper insights into deregulated metabolic pathways mediated by c-MAF. Here, we found the importance of c-MAF overexpression in MM cells for cell viability thereby contributing to MM pathogenesis. Abrogation of c-MAF deregulated sensitivity to glycolytic inhibitors and influenced metabolite readouts. Importantly, we established a quantitative metabolic profile of c-MAF driven MM using metabolomics to elucidate associated metabolic shifts, which identified purine metabolism to be significantly deregulated. Furthermore, purine metabolism was consistently identified to be perturbed in c-MAF driven MM by transcriptomics. Notably, nutrient starvation studies showed glutamine dependency in c-MAF overexpressed cells with potential implications on rate limiting enzymes linked to purine metabolism or metabolite transporters involved. The downstream identification of biological association of c-MAF with cancer metabolism may emerge as a new therapeutic strategy for MM patients known to have poor response to bortezomib. Taken together, our study suggests that metabolic perturbations present as a likely key Achilles heel in MM, and it could potentially shift the current treatment paradigm.

ID#41

Poster Presentation No. 18

An ex-vivo Combination Drug Sensitivity Platform for Predicting Sensitivity to FLT3 Inhibitor-based Combination in Acute Myeloid Leukemia

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Keywords: Acute Myeloid Leukemia, FLT3 mutation, Midostaurin, QPOP, drug sensitivity

Despite the increase in available treatment options for acute myeloid leukemia (AML) challenges remain in identifying patients who respond to a given regimen. Accurately predicting responses to treatment is crucial given the varying response rates to standard treatments, adverse effects and increasing drug cost. In this study, we explore the ability of an ex vivo drug sensitivity platform, quadratic phenotypic optimization platform (QPOP), in identifying potential responders and non-responders to possible combination therapies in FMS-like tyrosine kinase-3 (FLT3) mutant AML. We further investigate the mechanism behind selective sensitivity and resistance to FLT3 inhibitor-based combinations. AML cell lines were treated with a set panel of drugs recommended by physicians including FLT3 inhibitors (FLT3i). QPOP drug combination scores and ranking were derived from analysis of cell viability response following treatment with a series of test combinations. Molecular analysis was conducted to determine the accuracy of QPOP predicted response and FLT3 mutant status. Subsequently, we performed a prospective cohort pilot study of QPOP analysis with blood or marrow aspiration of AML patients. Patients were treated based on clinician guidance. The primary outcomes were to determine the ability of QPOP to predict sensitivity to FLT3i-based therapies. QPOP analysis on AML cell lines was accurately able to stratify FLT3i responders and non-responders including differential responses between an FLT3-ITD isogenic parental and FLT3i resistant line. QPOP accurately identified increased sensitivity to FLT3i-based combinations observed with a gain of FLT3-ITD mutation. Serial QPOP analysis in samples following midostaurin-based therapy indicated a decrease in FLT3i sensitivity was concordant with increasing FLT3 allelic burden and development of resistance. The development of resistance to FLT3i-based combinations was correlated to an increase in phosphorylated AKT expression in both AML cell lines and a patient sample. Further study of the potential mechanisms of acquired resistance to these combinations will be necessary.

ID#43

Poster Presentation No. 19

DDX6 - A potent A-to-I RNA Editing Repressor and an Immune Suppressor

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Keywords: A-to-I editing, *ADAR*, *DDX6*, Cancer, Innate immunity

Objectives: Adenosine Deaminases Acting on RNA (ADAR1p110, ADAR1p150 and ADAR2)-mediated A-to-I(G) editing is the most abundant RNA modification in mammals and is tightly regulated by non-ADAR proteins. Utilizing our ADARs co-IP/MS datasets, we identified the DEAD-box RNA helicase DDX6 as an ADAR-interacting protein. As both ADAR1 and DDX6 are known to regulate cell-intrinsic innate immunity, our study aims to elucidate the role of DDX6 in regulating A-to-I RNA editing and how DDX6-regulated editing events influence dsRNA-induced cell-intrinsic immunity in cancer.

Materials and Methods: RNA-sequencing was performed in DDX6-depleted cells to identify DDX6-regulated editing sites in an ESCC cell line, EC109. Cellular dsRNA was detected using dot blot with dsRNA-specific J2 antibody. eCLIP-seq was also performed to decipher the transcriptome-wide binding landscape of DDX6 in EC109 cells.

Results: We found that DDX6 interacts with all three ADAR proteins in EC109, but preferentially with the interferon-inducible ADAR1p150 isoform compared to the constitutively-expressed ADAR1p110 isoform. DDX6 functions predominantly as an A-to-I RNA editing repressor, with 93% (1095 out of 1172) of differential editing sites identified as being hyper-edited in DDX6-depleted cells. DDX6 depletion induces dsRNA accumulation in wild type but not in *ADAR1* KO cells, suggesting that ADAR1 is essential for DDX6-mediated dsRNA repression. Mechanistically, DDX6 preferentially binds to a 500-1000nt window downstream of DDX6-repressed editing sites situated at A-C mismatches as compared to those at A-U base-pairs. Furthermore, among editing sites with DDX6 binding at this window, there is a larger extent of editing repression by DDX6 at A-C sites where editing stabilizes dsRNA, over A-U sites where editing de-stabilizes dsRNA.

Conclusion: Taken together, our data suggests that *DDX6* functions as an oncogene by being an immune suppressor in cancer through repressing editing at A-C editing sites, which would otherwise become an I(G)-C base-pair and increase dsRNA stability when edited, triggering dsRNA-mediated immune activation.

ID#46

Abstracts Submitted

S/N	Name	Abstract Title
1	Samira Sadeghi	Bioorthogonal Catalysis for Treatment of Solid Tumors Using Thermostable, Self-assembling, Single Enzyme Nanoparticles and Natural Product Conversion with Indole-3-acetic Acid
2	Goh Jin Hao	Organ-based Three-dimensional Digital Modelling for Clinical Applications, Training and Medical Education
3	Nguyen Thuan Tinh	Variations in Cortical Functional Gradients Relate to Dimensions of Psychopathology in Preschool Children
4	Lu Zeyu	Providing Robots with The Human Sense of Touch
5	Woo Jun Yung	Overcoming Barriers for Clinical Translation of Non-virally Gene Modified Mesenchymal Stem Cells for Cell-directed Enzyme Prodrug Therapy (CDEPT)
6	Kenneth Yap Chun Hong	Gelsolin Hyperactivates WNT Signaling in Colorectal Cancer Cells Regardless of APC Mutation Status
7	Michelle Mak	Identification of a Novel Regulatory Element to Drive Robust Cardiac Specific Gene Expression
8	Tan Tze Xin Eunice	Dengue Precursor Membrane/Envelope Protein Influences *In-vivo* Virulence
9	Donald Ting Heng Rong	The Essential Role of N153-linked Glycan in DENV Pathogenesis
10	Maximilian Unfried	Designing Lifespan Extending Lipids with Deep Learning
11	Zijiao Chen	Deep Learning Based Continuous Vigilance Tracking from fMRI Data

Abstract

Bioorthogonal Catalysis for Treatment of Solid Tumors Using Thermostable, Self-assembling, Single Enzyme Nanoparticles and Natural Product Conversion with Indole-3-acetic Acid

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Keywords: thermostable, exoshell, protein encapsulation, bioorthogonal catalysis, tumor regression

Bioorthogonal catalysis (BC) generates chemical reactions not present in normal physiology for the purpose of disease treatment. Because BC catalytically produces the desired therapy only at the site of disease, it holds the promise of site-specific treatment with little or no systemic exposure or side effects. Transition metals are typically used as catalytic centers in BC; however, solubility and substrate specificity typically necessitate a coordinating enzyme and/or stabilizing superstructure for in vivo application. We report the use of self-assembling, porous exoshells (tESs) to encapsulate and deliver an iron-containing reaction center for the treatment of breast cancer. The catalytic center is paired with indole-3-acetic acid (IAA), a natural product found in edible plants, which undergoes oxidative decarboxylation, via reduction of iron(III) to iron(II), to produce free radicals and bioactive metabolites. The tES encapsulation is critical for endocytic uptake of BC reaction centers and, when followed by administration of IAA, results in apoptosis of MDA-MB-231 triple negative cancer cells and complete regression of in vivo orthotopic xenograft tumors ($p < 0.001$, $n = 8$ per group). When Renilla luciferase (rLuc) is substituted for horseradish peroxidase (HRP), whole animal luminometry can be used to monitor in vivo activity.

ID#19

Abstract

Organ-based Three-dimensional Digital Modelling for Clinical Applications, Training and Medical Education

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Keywords: Valve, Three-dimensional, Digitalization, Surgery, Education

Recent scientific breakthroughs and digital technological advancements have altered the way we diagnose and treat disease, resulting in transformation of the health care to be more accurate, predictable, and personalized to the individual patient. Cardiac valve diseases are commonplace within the field of medicine and thus involve a plethora of surgical methods that are subject to inaccuracies. Thus, there exists a need to standardize treatment methods through a template grounded by realistic and accurate parameters specific to the valve. This study aims to create an accurate digital three-dimensional model of the mitral and tricuspid valve. After preparation, negative impressions of the heart atrioventricular valves were created through introduction of a liquid that was frozen to produce a physical model. The solidified models were then scanned to produce digitalized three-dimensional models of the valves and associated structures. After intensive analysis of the valves' measurements, a three-dimensional model of the mitral and tricuspid annulus was obtained. Results gathered indicate a correlation between the anteroposterior diameter with mitral annulus circumference in the mitral valve, and between the posteroseptal diameter with tricuspid annulus circumference in the tricuspid valve. This study sets the foundation of the methodology in constructing a digital three-dimensional model of the valves based on the parameters obtained. Translating the methods to clinical setting would enable precise representation of the valves that could help surgeons tailor the cardiac valves specific to the individual patient. Anatomically accurate digital models of the patient's mitral and tricuspid valve would reduce estimations during surgeries and help the junior practitioners to make an informed decision on appropriate intervention approach. Outside of the surgical field, the digital model excels in its applicability to the medical educational field through their enhanced accessibility and validity in comparison to the current digital models used in medical education.

ID#22

Abstract

Variations in Cortical Functional Gradients Relate to Dimensions of Psychopathology in Preschool Children

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Keywords: Cortical Gradient, Preschool children, Psychopathology, Resting state functional magnetic resonance imaging

It is unclear how the functional brain hierarchy is organized in preschool children and whether alterations in the brain organization are linked to mental health in this age group. Here, we assessed whether preschool children exhibit a brain organizational structure similar to older children, how this structure might change over time and whether it might reflect mental health. This study derived functional gradients using diffusion embedding from resting state fMRI data of 4.5-year-old (N=100) and 6.0-year-old (N=133) children from the Growing Up in Singapore Towards healthy Outcomes dataset. We then conducted partial least square correlation analyses to identify the association between the impairment ratings of different mental disorders and network gradient values. The main organizing axis of functional connectivity (i.e., principal gradient) separated the visual and somatomotor regions (i.e., unimodal) in preschool children, while the second axis delineated the unimodal-transmodal gradient. This pattern of organization was relatively stable from 4.5 to 6 years of age. The second gradient separating the high- and low-order networks exhibited a diverging pattern across mental health dimensions, differentiating dimensions related to attention-deficit/hyperactivity disorder and phobic disorders. This study characterized for the first time the functional hierarchy in preschool children. A divergence in functional gradient pattern across different disease dimensions was found, highlighting how perturbations in functional brain organization can relate to the severity of different mental health disorders.

ID#24

Abstract

Providing Robots with The Human Sense of Touch

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Keywords: Tactile Sensing, Robotics, Human-Robot-Interaction

Aging society means less workers, farmers, and more elderly people in the next few decades, such as Japan and Singapore. Who will produce vehicles, food, or even take care of our elderly parents? Yes, robots. Industrial robots have been doing well in factories 24/7 for more than half a century. Recently, robots are entering our homes. However, robots of today lack safety, dexterity, and intelligence, making them unsuitable for these jobs. when We humans touch something, we know that contact information and do something with reactions. Tactile sensing is so important but is currently still missing in most robots. Therefore, I want to give robots that human sense of touch. My research focuses on developing a tactile sensor technology with a very thin normal force sensing layer and a 3D magnetometer pixel. This design gives the robots a soft feel, high resolution, and high sensitivity to small amounts of force, like human skin. My sensors are more than just pressure sensing. They measure all the tactile parameters that are essential for robots: such as contact location, slippery friction, global 3D force, and 3D torque. My sensors are customizable for both larger and smaller areas. I have integrated our sensors into a robotic hand. And my results show that these tactile sensor-enabled robots are not only able to perceive a sense of touch but also achieve some human-like skills, such as grasping daily objects with different shapes, sizes and stiffness, including delicate object like eggs, and handover objects by combining AI algorithms. Once again, my research aims to address the future need the aging society, we are facing in the next few decades. I want to give robots the human sense of touch and make robots capable of taking care of our elderly parents at homes in the future.

ID#25

Abstract

Overcoming Barriers for Clinical Translation of Non-virally Gene Modified Mesenchymal Stem Cells for Cell-directed Enzyme Prodrug Therapy (CDEPT)

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Keywords: Mesenchymal stem cells, Transfection, CDEPT, Cell burden, Cryopreservation

Objectives: The advent of cell and gene therapy has culminated in the development of many new and innovative therapies for the treatment of a myriad of diseases. Our lab has been developing solutions for the industrialization of non-viral precision gene engineered MSCs as bio-factories, offering clinical solutions in oncology and regenerative medicine. Increasingly, engineered mesenchymal stem cells (MSCs) have been reported to provide a safer and more potent cancer therapy than heterogenous native MSCs. These highly efficiently engineered cells carry significantly higher therapeutic payloads (a suicide gene, cytosine deaminase) and showed higher potency than lentiviral modified equivalents. The next step is to effectively scale-up in production and preserve these therapeutic cells for rapid deployment.
Materials and Methods: Using a novel scale-up approach, we successfully increased the productivity per-culture-area by over 5-fold. We have also developed a DMSO-free reagent that preserve cell viability at >90% post thaw and is compatible for direct injection, minimizing the need for additional handling that could introduce unwanted variability.
Results: These engineered cells have now been used to treat cancers in no-option-left companion animals with favourable results, where recurrence did not happen over a prolonged period (>2 years). Efficient storage of the cells by cryopreservation was achieved and is essential to create an off-the-shelf solution that not only allows us to reach a wider patient pool but also offers assurance of safety by allowing greater quality control testing and standardization. Some of the challenges in this endeavor is the burden of cellular stress due to exceptionally high overexpression of transgene and its effects on cryopreservation. To this end, attempts were made to identify unbiased transcriptomic changes related to these challenges which led to significant mitigation using pharmacological interventions.
Conclusions: This body of work set the stage for the successful translation of MSC-based therapeutics closer to use in clinic.

ID#27

Abstract

Gelsolin Hyperactivates WNT Signaling in Colorectal Cancer Cells Regardless of APC Mutation Status

Yap KCH[1,2,3], Ong MS[2,3], Okina E[1,3], Datta A[3,4], Shanmugam MK[1,3], Deng S[2,3], Tan TZ[4], Tolwinski N[5,6], Sethi G[1,3], Kumar AP[1,3,*], Yap CT[2,3,*]

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Keywords: Gelsolin, colorectal cancer, Wnt/β-catenin, epithelial to mesenchymal transition, metastasis

Objectives: Activation of Wnt signaling is among the earliest events in colon cancer development. It is achieved either via activating mutations in the CTNNB1 gene encoding β-catenin, the key transcription factor in the Wnt pathway, or through inactivating mutations in APC, a major negative regulator of β-catenin. In our effort to identify non-mutational hyperactivating events, our RNA Seq analysis showed overall Wnt hypoactivation in gelsolin knock out mice.

Materials and Methods: Pre-processed data downloaded from AffyExpress. Genes involved in WNT were curated and heatmaps generated. Overexpression of gelsolin RNAi was used to inhibit gelsolin expression in Drosophila models. A volume of 0.2ml tumor cells was used as inoculum into the subcutaneous tissue of NOD SCID mice. Gelsolin-overexpressing, knock-down and mutant gelsolin deficient in severing activity *invitro* models were used to examine the causal relationship between gelsolin and Wnt/β-catenin signaling.

Results: Having observed significant changes in expression of regulators of Wnt and EMT processes from an RNA Seq data comparing gelsolin knock out mice to wild type mice, we seeked to validate this finding in mice and *Drosophila* models. Overexpression of gelsolin increased primary tumor volume, promoted tumor metastasis and attenuated iCRT3-induced reduction of tumor volume. This was further strengthened *in-vivo* where gelsolin knockdown reduced cell polarity and Wnt activity. We show that differential expression of gelsolin led to changes in Wnt-induced polarization, accompanied by changes in EMT genes in a variety of *in-vitro* assays. Interestingly, overexpression of gelsolin stabilizes cytoplasmic pool of β-catenin, thereby promoting β-catenin nuclear translocation and increased Wnt activity. We narrowed this activity to gelsolin's F-actin binding and severing domain.

Conclusion: Common APC mutations activate Wnt signaling in colorectal cancers. Here we demonstrate that further potentiation of this pathway involves the ability of gelsolin to allow for increased cytoplasmic β-catenin accumulation, leading to increased nuclear Wnt activity.

ID#30

Abstract

Identification of a Novel Regulatory Element to Drive Robust Cardiac Specific Gene Expression

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[1]*Cardiovascular Research Institute, National University Health System, Singapore*
Keywords: Genomics, adeno-associated viruses

In this study, we aimed to identify a novel regulatory element capable of driving robust cardiac specific gene expression, utilising adeno-associated viruses (AAVs) as a model system. The first part of the study centres on the hypothesis that we can identify cardiac cell-type specific regulatory elements (CREs) through bioinformatics analysis, and such elements can drive specific and robust expression of transgenes in combination with an appropriate AAV capsid. In line with this, we established a bioinformatics workflow to shortlist potential candidate regions. Briefly, datasets from the Human Protein Atlas, GTEX, and Genevestigator were examined, and heart specific genes identified. In total, 4 genes were identified to be common in all 3 databases interrogated. We shortlisted 58 genomic loci associated with the 4 genes using data from the Activity-by-Contact model and H3K27ac ChIP-Seq in the Foo lab. These were further shortlisted to 18 loci after evaluation of H3K27ac peaks in various organs (ENCODE data). Each CRE was then cloned upstream of a minimal promoter driving the expression of GFP or luciferase reporter gene and AAVs then produced according to standard protocol. *In vitro* luciferase assays conducted with the Dual-Glo luciferase assay system (Promega) in HEK cells revealed that CREs 2, 3, 6, 12, 17, and 18 were observed to have lower expression in HEK cells as compared to the cTNT promoter that acted as our basis of comparison. As such, they were shortlisted for further *in vivo* experiments in p10 mice. Preliminary data from p10 mice suggests that some of the identified CREs do possess cardiospecificity. We aim to further characterise these regulatory elements and potentially develop a highly cardiac-specific regulatory element that can drive robust gene expression.

ID#31

Abstract

Dengue Precursor Membrane/Envelope Protein Influences *In-vivo* Virulence

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Keywords: Dengue, envelope, precursor membrane, virulence

Dengue virus (DENV) comprises of three structural (capsid, precursor-membrane, envelope) and seven non-structural proteins (NS1 to NS7). Of its structural proteins, the precursor membrane and envelope (prM/E) proteins form the glycoprotein shell of the virus that interacts with the host cell surface. Previous work in the laboratory has shown that prM/E plays a critical role in the in vivo fitness of D2Y98P, a representative DENV2 strain that circulates in South East Asia. To further investigate the role of prM/E in DENV virulence, a chimerisation approach was adopted where prM/E from D2Y98P was replaced with that from non-virulent DENV1 and from non-virulent DENV2, NGC, giving rise to DENV1-2 and NGC-D2Y chimeras respectively. Infection kinetics in vitro in both mammalian and mosquito cell lines indicated that the chimeric viruses displayed comparable fitness with D2Y98P WT, suggesting that viral entry and replication were not affected by the chimerisation. In IFNAR-/- mice however, both chimeric viruses displayed marked attenuation, as evidenced by increased survival rate, lower viral loads, and lower levels of pro-inflammatory cytokines compared to D2Y98P-infected mice. Taken together, these findings indicate that replacing the prM/E region with a non-virulent variant, across serotype and within genotype, resulted in in vivo attenuation of the virus, supporting the hypothesis that prM/E drives virulence.

ID#39

Abstract

The Essential Role of N153-linked Glycan in DENV Pathogenesis

Ting DHR[1], Idris FFH[1], Tan TXE[1], Wan C[2], Choo MSF[2], Koh CWT[3], Chan KR[3], Walsh I[2], Nguyen-Khuong T[2], and Alonso S[1]

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Keywords: Dengue virus, N-linked glycosylation, antibody

Dengue virus (DENV) poses a huge disease burden globally with an estimated 390 million infections annually. The main viral structural protein, envelope protein (E), is a promising sub-unit vaccine candidate. It is glycosylated at two asparagine (N) sites (N67 and N153), but its glycosylated variants and their biological importance have been largely overlooked. Using reverse genetic, we have generated a partially deglycosylated DENV mutant that lacks glycan structures at N153 (N153Q). The *in vitro* and *in vivo* fitness of the mutant was studied. Our data show that the N153Q mutant grown in mosquito larvae homogenate cells (C6/36) and baby hamster kidney cells (BHK-21) was as fit as wildtype (WT) virus but was impaired in human hepatocyte (Huh-7) and non-human primate kidney epithelial cells (Vero). Besides, N153Q mutant was greatly attenuated in mice, as evidenced by milder clinical manifestations and lower virus titers both in circulation and specific organs (kidney and liver). Whole blood transcriptomic data suggested that there was no difference in the host responses to infection with WT and N153Q strains. Interestingly, N153Q virus was found to be neutralized more effectively by sera from convalescent dengue patients compared to WT, suggesting that glycan motifs on N153 position shield DENV from antibody binding and neutralization. Consistently, B cell depletion significantly restored the viremia in N153Q-infected mice. In conclusion, our findings provide novel insights on the role of N153-linked glycan in DENV pathogenesis, with potential implications for the development of effective therapeutic antibodies, vaccine candidates and anti-viral drugs.

ID#40

Abstract

Designing Lifespan Extending Lipids with Deep Learning

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Keywords: lipids, aging, deep learning, cellular reprogramming, artificial intelligence

The known lipid universe consists of a heterogenous group of hydrophobic or amphipathic molecules. Through signaling, bioactive lipids play crucial roles in metabolism, diseases, and aging. Moreover, signaling lipids have been found to modulate organismal longevity by triggering mechanisms responsible for slowing and delaying aging. Lipids such as 17a-estradiol and Dihomo-γ-linolenic acid, have been shown to extend health- and lifespan in model organisms. Furthermore, lipids like Methylprednisolone and Forskolin are commonly found in cellular reprogramming cocktails. This begs the question – can we design novel lipids with similar properties? In this *In Silico study* we use generative deep learning methods to generate novel lipids that have structural similarities and characteristics to lipids that have beneficial effects on health-and lifespan.

ID#12

Abstract

Deep Learning Based Continuous Vigilance Tracking from fMRI Data

Chen Z[1], Ng KK[1], Liu S[1,2], Wang C[1,2], Soon CS[1,2], Yeo BTT[1,2,3], Ong JL[1], Chee MML[1,2], Zhou JH[1,2,3*]

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Keywords: Multi-Modal Imaging, BOLD fMRI, EEG, Methods Development, Sleep and Wakefulness

Objectives: Fluctuations in vigilance can affect behavioral responses and brain functional signals and should be accounted for in fMRI studies. EEG is an objective marker for vigilance fluctuation. However, concurrent EEG-fMRI is not always feasible. Therefore, predicting vigilance directly from fMRI signals would be useful to address the effect of arousal fluctuations, which could in turn enhance our understanding of neurocognitive processes. To this end, we aim to propose a deep learning approach to predict vigilance fluctuation directly from BOLD time series with EEG-defined vigilance as the ground truth, across different age groups, different experimental conditions and different arousal states.

Materials and Methods: Simultaneous EEG-fMRI scans during both RS and Task conditions were obtained from young adults, elderly and adolescents in RW and SD. BOLD timeseries were extracted from cortex, subcortex and brainstem. The alpha slow wave index was derived from EEG as the vigilance benchmark. The BOLD timeseries were feed as input and ASI as target output into the neural networks for each state-condition dataset. We next performed transfer learning to learn the target data distribution and increase the generalizability of the model. Lastly, to determine the contribution of each brain network to vigilance prediction, we performed a feature importance analysis.

Results: The proposed model predicted fluctuations in vigilance from fMRI across all conditions. Through transfer learning, our model can adapt from one data domain to another efficiently. Feature importance analysis showed that the thalamus and brainstem were the most significant predictors in all the conditions. Vigilance was also largely predicted by higher-order cognitive networks including the DMN, salience, dorsal attention and executive control networks.

Conclusions: The proposed deep learning model can predict vigilance fluctuations from fMRI directly. We have demonstrated its generalizability across task and different mixtures of arousal state in healthy young adult, elderly and adolescents.

ID#28

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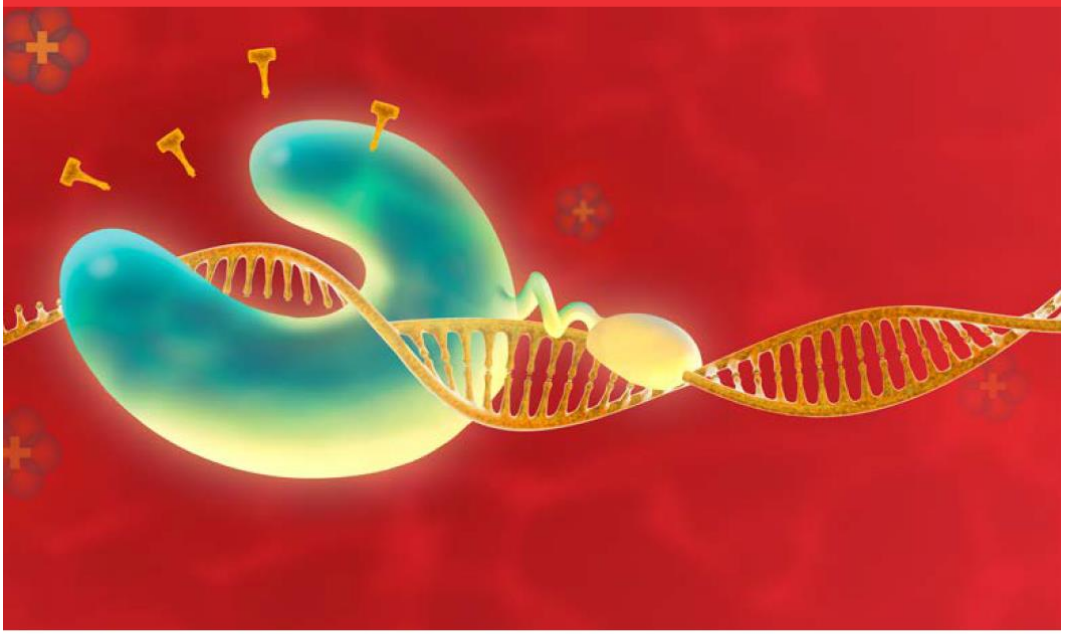

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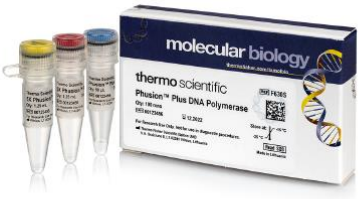

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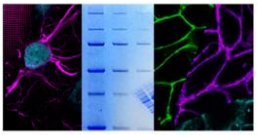

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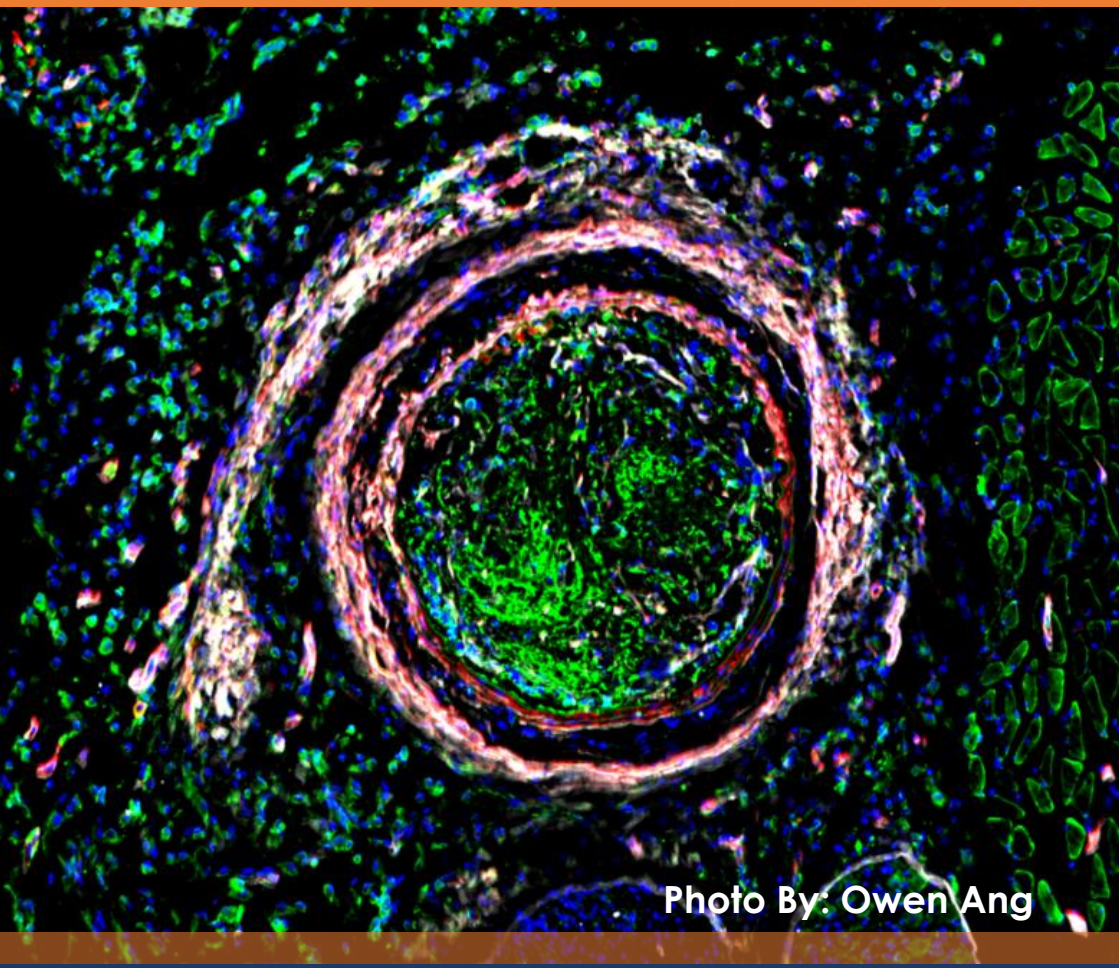

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