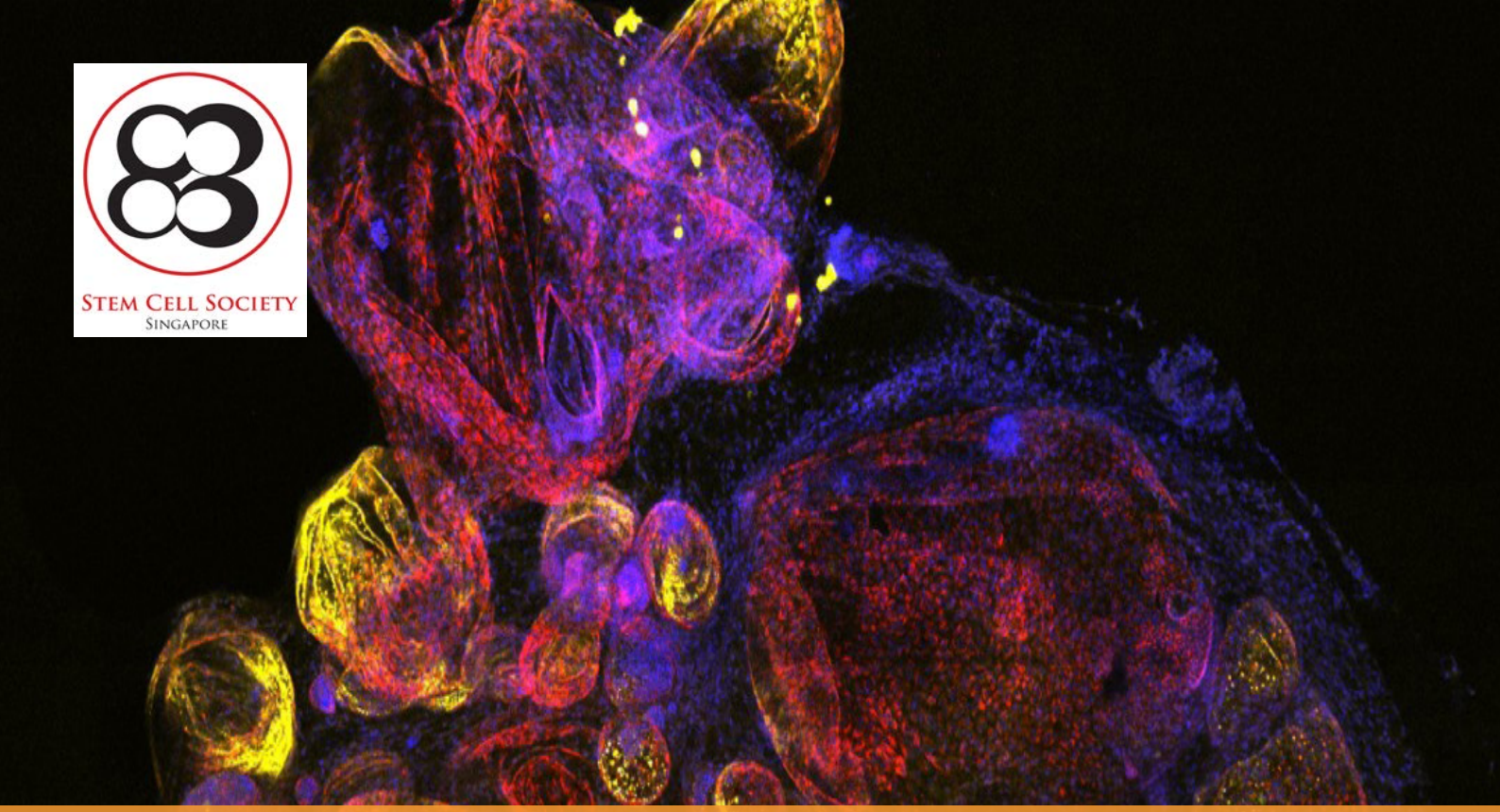


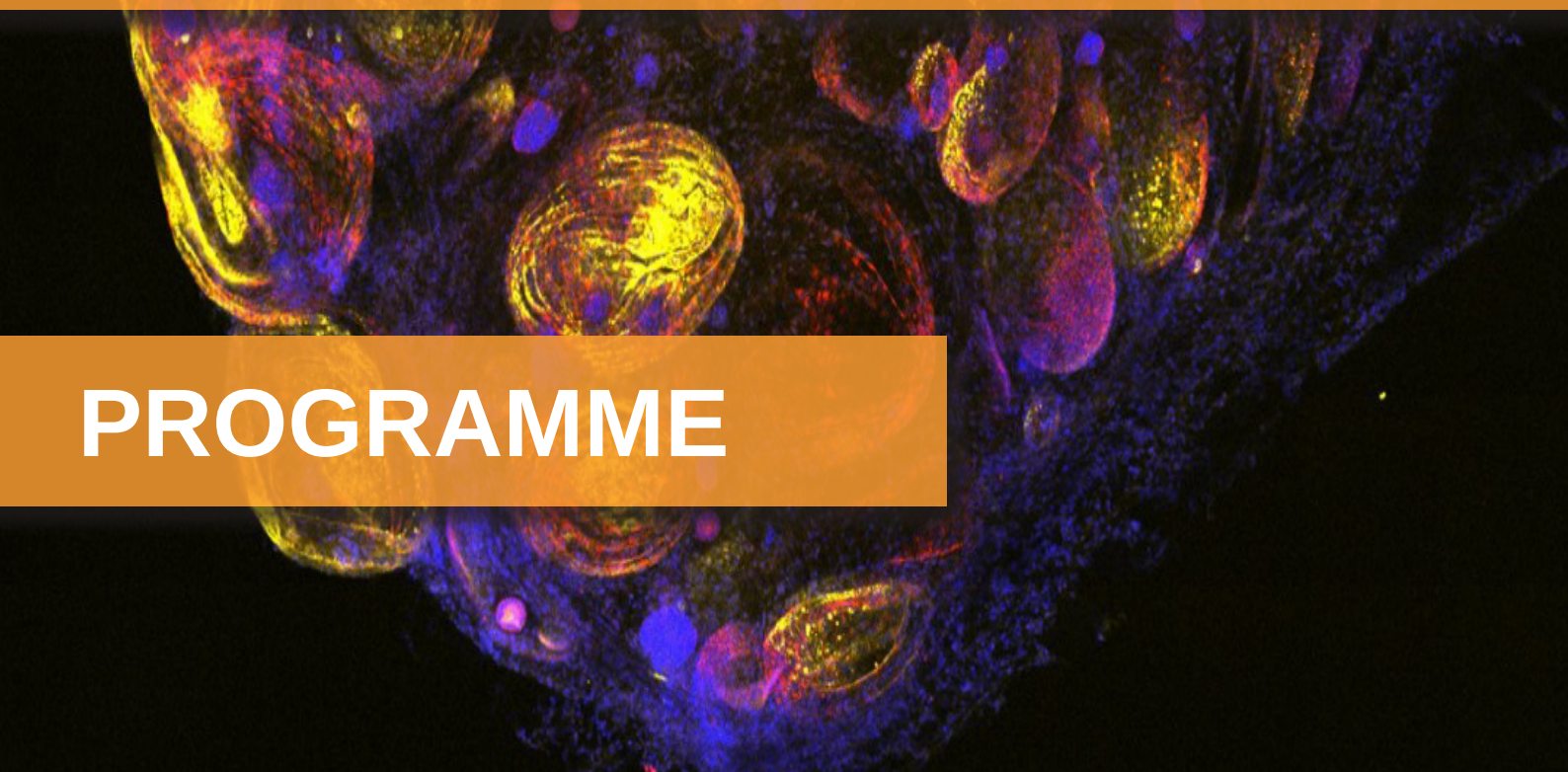
STEM CELL SOCIETY
SINGAPORE

17th Annual Symposium 2025

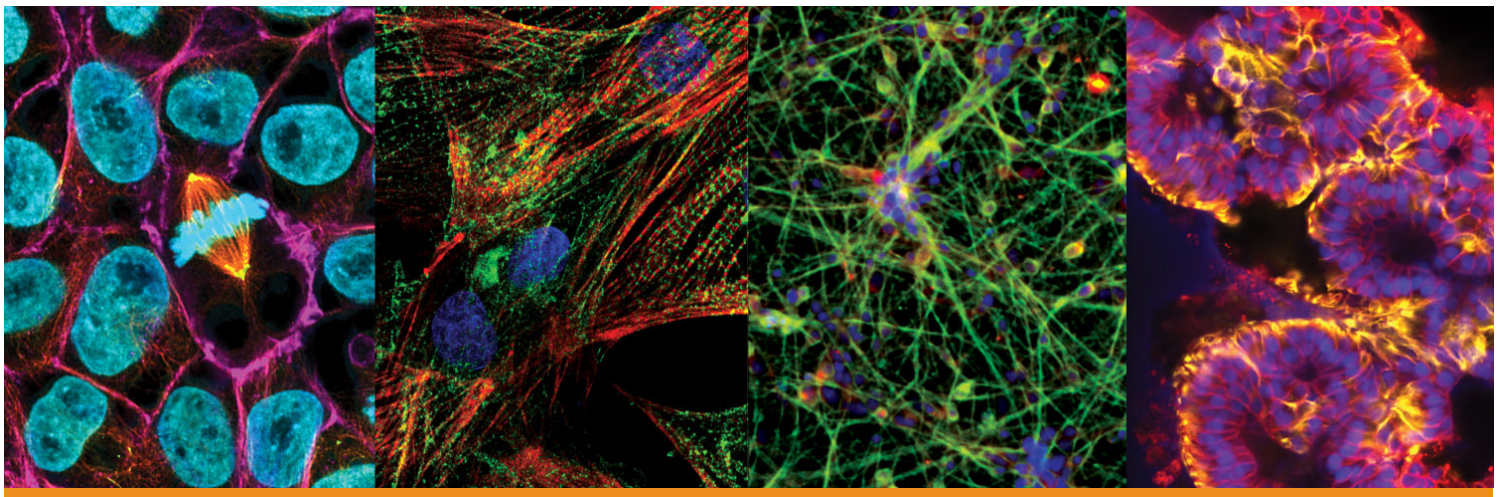
Stem Cell Society Singapore

11 - 14 November

Auditorium, Matrix @Biopolis



PROGRAMME



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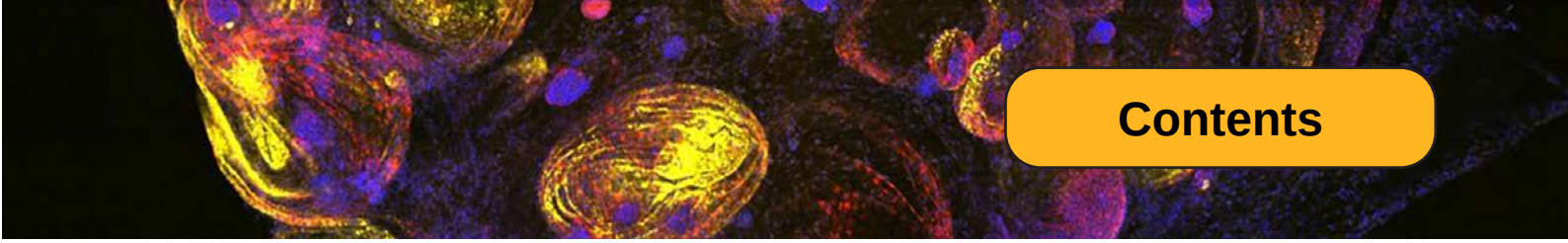

Contents

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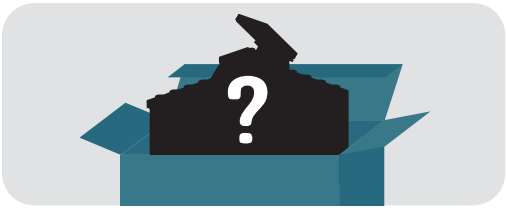

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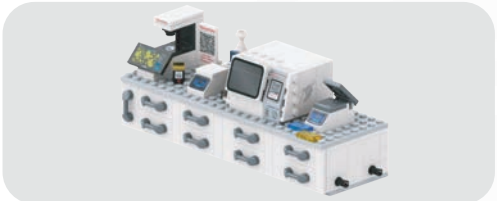

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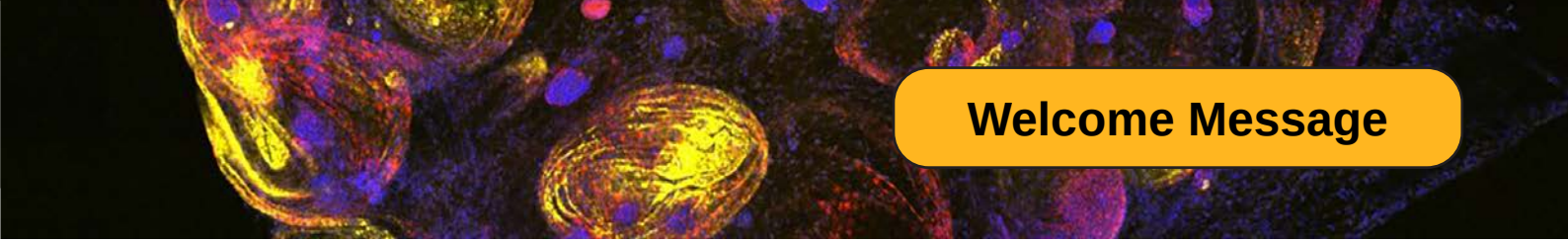

Welcome Message

Dear Colleagues & Friends,

A warm welcome to the 17th Stem Cell Society Singapore (SCSS) Symposium 2025 in the beautiful city of Singapore. We are thrilled to host you here at Biopolis, the site of our first symposium.

As SCSS's flagship event, this symposium reflects our dedication to fostering collaboration and advancing stem cell research. This year, we bring together a diverse international group of experts from academia, industry, and clinical sectors to share ideas, experiences, and pioneering discoveries.

In response to the rapid field evolution, our program covers a wide range of basic and translational research, including organoid disease modeling, stem-cell-based cardiac models, epigenetic regulation of early embryonic fate, vascular and metabolic diseases, and cell therapeutics.

We are proud to host two distinguished keynote speakers: Prof. Martin Pera (Jackson Laboratory, USA) and Prof. Duanqing Pei (Westlake University, China), whose expertise exemplifies the high-caliber discussions we aim to foster.

Additionally, for the first time, we will feature the AASCRM (Asian Alliance of Stem Cell and Regenerative Medicine) lectures, with speakers from China, Japan, and Korea, further strengthening regional collaborations.

The symposium will also feature a dedicated poster session to showcase emerging research. Our sincere thanks to all speakers, sponsors, and especially Dr. Susan Lim, for her ongoing support of the SCSS-Dr. Susan Lim Award for Outstanding Young Investigator. Special appreciation goes to our volunteers for ensuring the smooth organization of this event.

We look forward to your active participation, enriching discussions, and fostering new collaborations. We hope you leave inspired and enlightened by this shared journey.

With warm regards,
The Organizing Committee

Jonathan Loh (Chair)
Matias Autio
Nadia Omega Cipta
Shigeki Sugii
Hwee Goon Tay
Gerald Udolph
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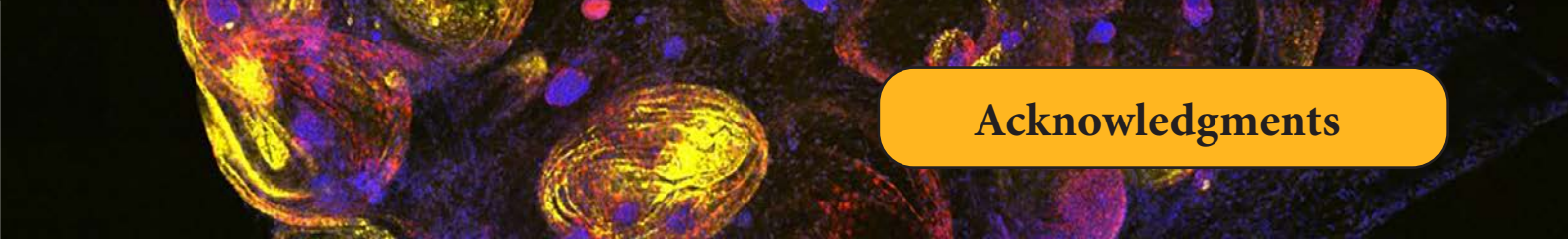

Acknowledgments

We wholeheartedly thank our corporate members, exhibitors, and supporters for their generous contributions. Their participation is crucial to bringing this symposium to life.

Please visit the exhibitors' booths to explore their products, participate in raffles, and interact with their representatives.

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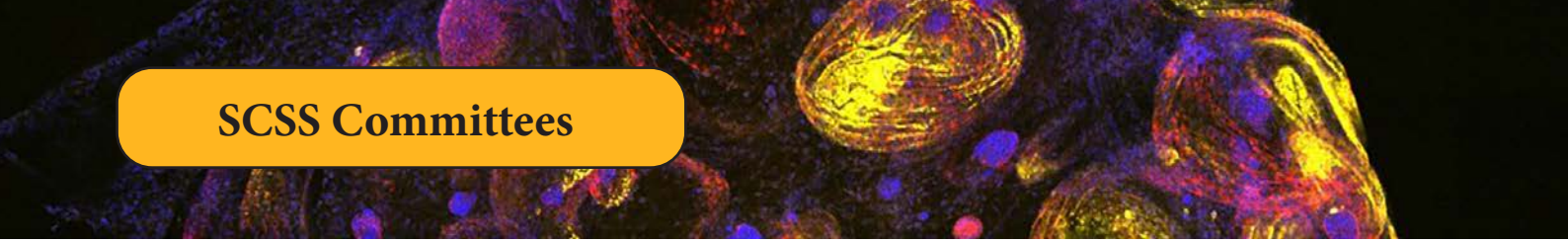

SCSS Committees

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Shigeki **SUGII** (*A*STAR Singapore Institute of Food and Biotechnology Innovation& Secretary SCSS*)

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Gerald **UDOLPH** (*Stem Cell Society Singapore*)

Yun **XIA** (*NTU, Lee Kong Chian School of Medicine, Singapore*)

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Andy TAY (*National University of Singapore*)

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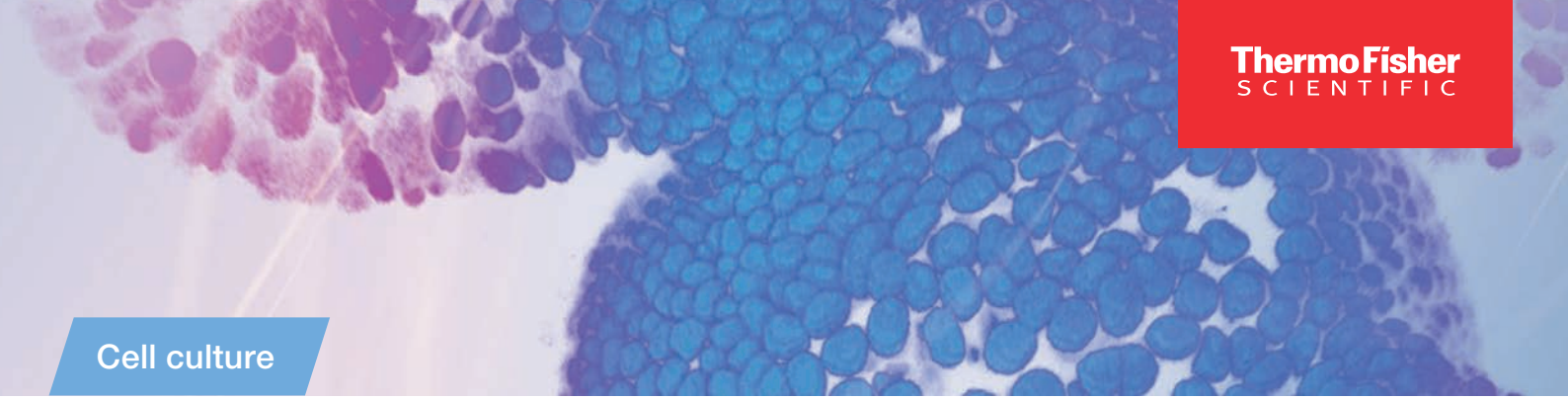
Fengwei YU (*TSL, Singapore*)



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		10 mL	A4000046703
Stem cell culture	Geltrex Flex LDEV-Free hESC-Qualified Reduced Growth Factor Basement Membrane Matrix	1 mL	A4000046801
		5 mL	A4000046802
		10 mL	A4000046803
Organoid cell culture	Geltrex Flex LDEV-Free Organoid-Qualified Reduced Growth Factor Basement Membrane Matrix	1 mL	A4000046901
		5 mL	A4000046902
		10 mL	A4000046903

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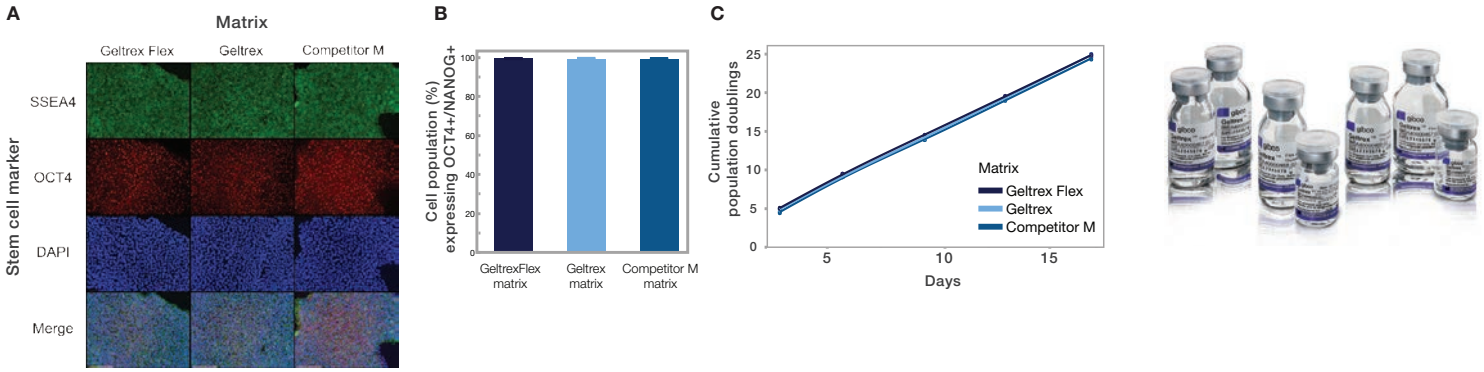

Figure 2. hiPSCs grow and maintain pluripotency on hESC-qualified Geltrex Flex, Geltrex, and competitor M's matrices. Assessed parameters included cell morphology, growth and expansion, pluripotency marker expression, viability, gene expression, and neural stem cell induction. **(A)** OCT4/SSEA4 marker expression. **(B)** OCT4/NANOG co-localization. **(C)** Cumulative population doublings over five passages ($p \leq 0.05$) of hiPSCs cultured on the different matrices.

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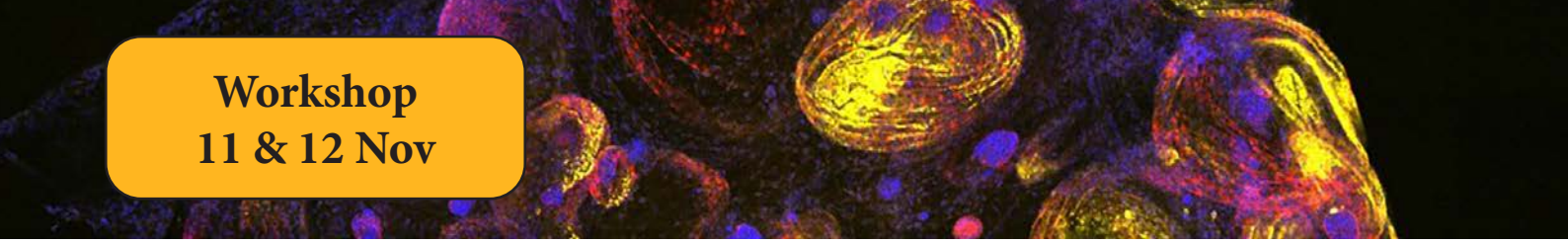
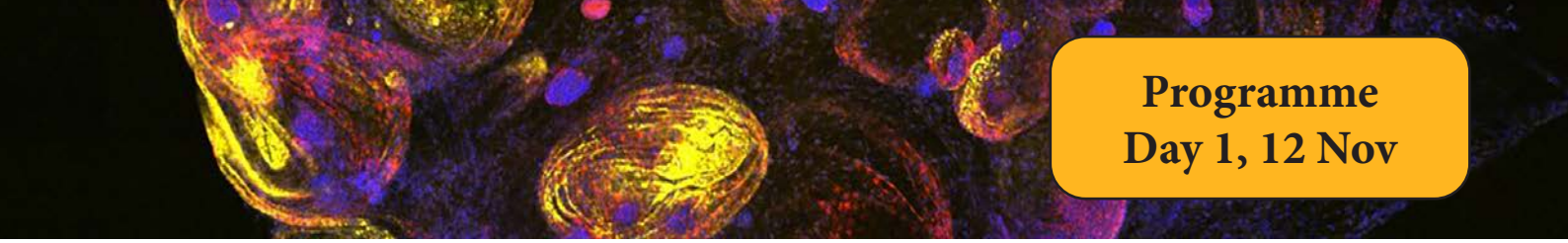
Programme



Workshop
11 & 12 Nov

Time	DAY 1 (Tuesday, 11 Nov 2025)		DAY 2 (Wednesday 12 Nov 2025)	
	Programme	Venue	Programme	Venue
8:00	Registration	Aspiration Theatrette, Matrix, L2M	Parallel hands-on session*: A) ThermoFisher B) STEMCELL Tech	Session A: ThermoFisher CEC Session B: IMCB, Proteos building
8:45 - 9:00	Welcome address			
9:00 - 9:30	Ice-breaking session			
9:30 - 10:00	**Lecture 1: Embryonic stem cells & early development**			
10:00 - 10:30	*Lecturer: Martin Pera*			
10:30 - 11:00	Break			
11:00 - 11:30	**Lecture 2: iPSC & reprogramming**			
11:30 - 12:00	*Lecturer: Yuin-Han Loh, Jonathan*			
12:00 - 12:30	**Lecture 3: Adult stem cells & organoids**			
12:30 - 13:00	Subtopic 1: Intestinal stem cells *(Lecturer: Bon-Kyoung Koo)* Subtopic 2: Muscle stem cells *(Lecturer: Reshma Taneja)* Subtopic 3: Neural stem cells *(Lecturer: Alfred Sun)*			
13:00 - 13:30	Lunch			
13:30 - 14:00				
14:00 - 14:30	**Lecture 4: Directed differentiation & transdifferentiation**		SCSS Symposium**	Auditorium, Matrix, L2
14:30 - 15:00	*Lecturer: Xia Yun*			
15:00 - 15:30	**Lecture 5: Stem cell manufacturing for cell therapy**			
15:30 - 16:00	*Lecturer: Jaichandran Sivalingam*			
16:00 - 16:30	Break			
16:30 - 17:00	**Lecture 6: Stem cell-based clinical trials**			
17:00 - 17:30	*Lecturer: Yap Eng Soo*			
17:30 - 18:00	Professional development session	IMCB Event Room, Proteos, L7		
18:00 - 18:30				
18:30 - 19:00	Networking session (with lecturers and invited industry scientists)			
19:00 - end				



Programme Day 1, 12 Nov

13:30 – 13:35 **Welcome & opening of Symposium 2025**
Jonathan Yuin-Han LOH, *Institute of Molecular & Cell Biology, Singapore & President SCSS*

Session 1. Cell therapeutics & clinical translation

This session is supported by the
DUKE-NUS MEDICAL SCHOOL, SINGAPORE
Chair: Hwee Goon TAY, *Duke-NUS Medical School, Singapore*

13:35 – 14:05 **Peripheral hematopoietic intervention to rescue neurodegeneration in the brain**
Helen GOODRIDGE, *Cedars-Sinai Medical Center, USA*

14:05 – 14:35 **Functional genomics of diabetes using hPSC-derived islet-like cells**
Adrian TEO*, Institute of Molecular & Cell Biology, Singapore*

14:35 – 15:05 **AASCRM LECTURE – Chinese Society for Stem Cell Research**
In Utero stem cell transplantation: from functional characterization to disease modelling and therapeutic exploration
Fanyi ZENG, *Shanghai Jiao Tong University School of Medicine, China*

15:05– 15:30 AFTERNOON TEA BREAK

15:30 – 15:45 *Selected Abstract*
Induced macrophage-kidney organoids unravel context-dependent immune modulation in kidney development and disease
Huaming WANG, *LKCM, Nanyang Technological University, Singapore*

15:45 – 16:00 *Selected Abstract*
Hypoimmunogenic retinal pigment epithelial cells promote immune tolerance for off-the-shelf retinal regenerative therapy
Asfa ALLI-SHAIK, *Institute of Molecular and Cell Biology, Singapore*

16:00 – 16:30 **Corneal endothelial cell therapy: Current practise**
Dr Jodhbir Singh MEHTA, *Singapore Eye Research Institute, Singapore*

Session 2. Thermo Fisher Scientific Mini-Symposium “Harnessing iPSC technology for drug discovery, disease models, and beyond”

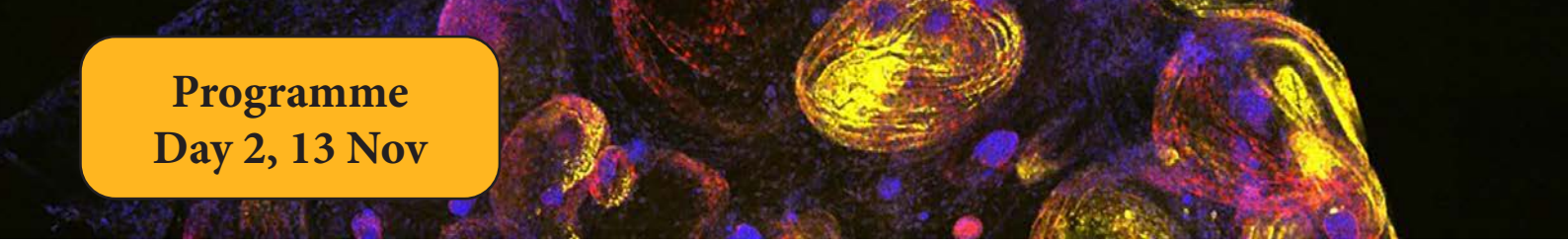
Chair: Poh Loong SOONG, *Thermo Fisher Scientific, Singapore*

16:30 – 17:00 **Effective targeted transgene knock-in & expression in hPSCs**
Matias AUTIO, *Genome Institute of Singapore*

17:00 –17:15 **Microphysiological systems: Development of vascularized tumor models for immunotherapy**
Geetika SAHNI, *AIM Biotech, Singapore*

17:15 –17:30 **iPSC-iNK workflow solutions for scalable cell therapy manufacturing**
Ryan LIM, *Thermo Fisher Scientific, Singapore*

17:30 – 19:00 POSTER SESSION WITH WINE & CHEESE
END OF DAY 1



Programme
Day 2, 13 Nov

9:00 – 09:30 **NHCS AGILENT MOU SIGNING CEREMONY**

Session 3. Epigenetic dynamics of early embryonic fate

This session is supported by the
INSTITUTE OF MOLECULAR AND CELL BIOLOGY (IMCB), SINGAPORE
Chair: Jonathan Yuin-Han LOH, *IMCB, Singapore*

9:30 – 10:15 **KEYNOTE LECTURE**
Sall4 dependent chromocenter remodeling and cell fate control
Duanqing PEI, *Westlake University, China*

10:15 – 10:45 **Indispensable role of ERK signal in the self-renewal and differentiation of embryonic stem cells**
Lingyi CHEN, *Nankai University, China*

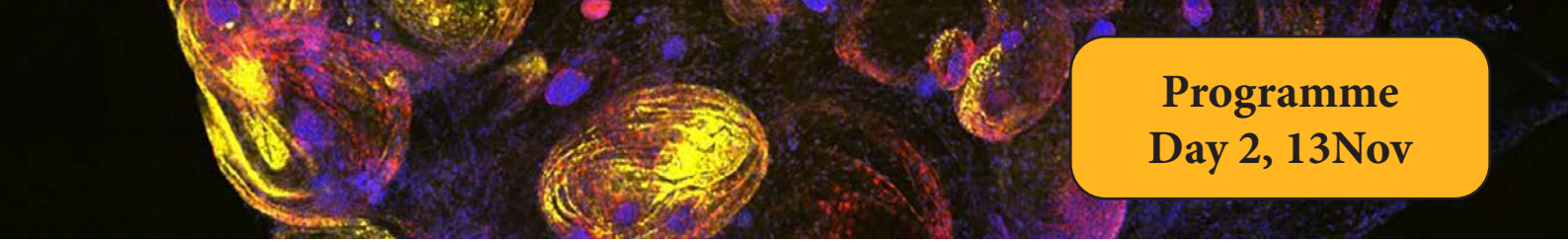
10:45 – 11:15 MORNING TEA BREAK

11:15 – 11:30 *Selected Abstract*
Single-cell m6A atlas decodes dynamic epitranscriptomic programs that orchestrate cell fates throughout development
Kiyofumi HAMASHIMA, *Institute of Molecular and Cell Biology, Singapore*

11:30 – 11:45 *Selected Abstract*
Decoding the genetic landscape of human evolution
Richard SHE, *School of Biological Sciences, Nanyang Technological University, Singapore*

11:45 – 12:15 **Long-term expandable mouse and human chondroprogenitor cells achieve functional cartilage repair in vivo**
Ronghui LI, *National University of Singapore*

12:15 – 13:30 LUNCH BREAK



Programme Day 2, 13Nov

Session 4. Stemcell Technologies Mini-Symposium

Chair: Robert Neil JUDSON, *STEMCELL Technologies Inc, Canada*

13:30 – 13:50 **A novel mRNA-lipid nanoparticle platform to rapidly generate functional forebrain neurons from human pluripotent stem cells using NGN2**
Robert Neil JUDSON, *STEMCELL Technologies Inc, Canada*

13:50 –14:10 **Single-cell multiomics identifies chromosome 21 regulators of intellectual disability genes in Down Syndrome**
Vincenzo DE PAOLA, *Duke-NUS Medical School, Singapore*

14:10 –14:30 **Decoding human neurodegeneration using stem cells**
Rickie PATANI, *National University of Singapore*

Session 5. Stem cells in vascular biology and metabolism

Chair: Shigeki SUGII, *Singapore Institute of Food and Biotechnology Innovation, Singapore*

14:30 – 15:00 **Harnessing endothelial cell plasticity to restore tissue homeostasis**
Christine CHEUNG, *Nanyang Technological University, LKCM, Singapore*

15:00 – 15:30 **AASCRM LECTURE – Japanese Society for Regenerative Medicine**
Strategic development of next-generation artificial platelets informed by reverse translational research
Koji ETO, *CiRA, Japan*

15:30 – 16:00 AFTERNOON TEA BREAK

16:00 – 16:30 **Metabolic programming of muscle stem cells and muscle organoids**
Shyh Chang NG, *Institute of Zoology, Chinese Academy of Sciences, China*

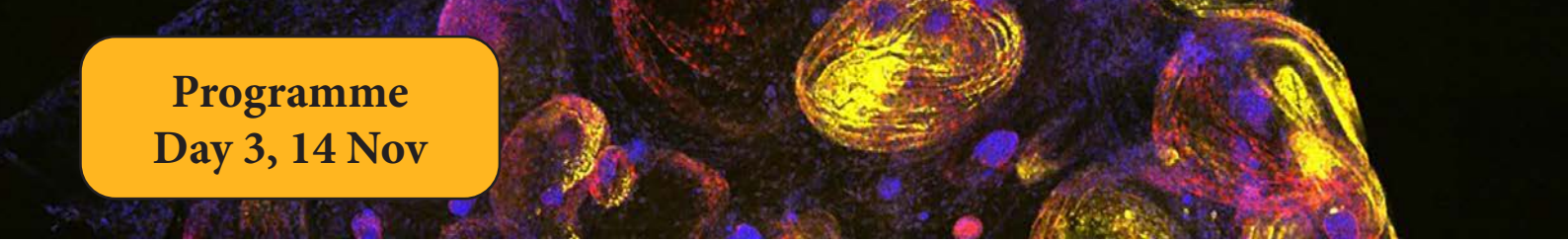
16:30 – 16:45 *Selected Abstract*
Making platelets from human adipose tissue-derived mesenchymal cells and the effect on a GVHD model using NOG mice
Yumiko MATSUBARA, *Keio University, Japan*

16:45 – 17:00 *Selected Abstract*
VHL deficient human kidney organoid to model clear cell renal cell carcinoma
Yixuan WANG, *Nanyang Technological University, LKCM, Singapore*

17:00 – 17:30 **Vascular niches of the bone marrow: Regulators of stem cell ageing and regeneration**
Anjali KUSUMBE, *Nanyang Technological University, LKCM, Singapore*

17:30 – 18:15 **SCSS-Dr Susan Lim Award for Outstanding Young Investigator Presentation**
Chair: Jonathan Yuin-Han LOH, *Institute of Molecular & Cell Biology, Singapore*
Biomaterials to engineer human immune cells and tissues
Andy TAY, *National University of Singapore*

18:15 END OF DAY 2



Programme
Day 3, 14 Nov

Session 6. Organoid disease modeling

Chair: Yun XIA, *Nanyang Technological University, LKCM, Singapore*

This session is supported by the
LEE KONG CHIAN SCHOOL OF MEDICINE (LKCM), SINGAPORE

9:00 – 9:30 **A decade of human midbrain-like organoids: Advances, discoveries, and future directions in Parkinson's Disease modeling and therapy**
Shawn JE, *Duke-NUS*, *Singapore*

9:30 – 10:00 **Novel roles of the epigenetic repressor SMCHD1 in regulating spermatogonial stem cell maintenance**
Shifeng XUE, *National University of Singapore*

10:00 – 10:30 **Refining human brain organoid models to capture human-specific features**
Hongyan WANG, *Duke-NUS, Singapore*

10:30 – 11:00 MORNING TEA BREAK

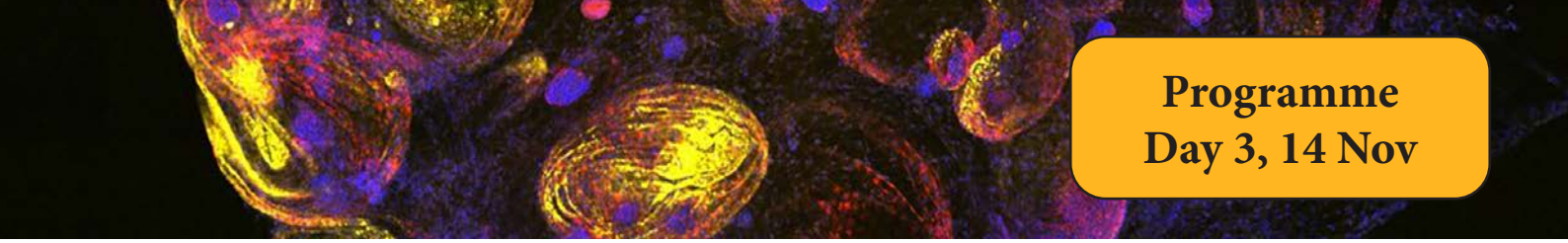
11:00 – 11:15 **Epithelial WNT secretion drives niche escape of developing gastric cancer**
Ji-Hyun LEE, *Institute for Basic Science, Republic of Korea*

11:15 – 11:30 *Selected Abstract*
Investigating thymic involution through thymic organoids
Jia Ming Nickolas TEO, *Institute of Molecular and Cell Biology, Singapore*

11:30 – 12:00 **AASCRM LECTURE – Korean Society for Stem Cell Research**
Organoids Zoo - a new platform for animal science
Bon-Kyoung KOO, *Institute for Basic Science, Republic of Korea*

12:00 – 12:15 **SCSS – ASSCR MOU SIGNING CEREMONY**
Jonathan Yuin-Han LOH, Institute of Molecular & Cell Biology, Singapore & President SCSS
Lincon STAMP, University of Melbourne, Australia & President ASSCR, Australia

12:15 – 13:30 LUNCH BREAK



Programme Day 3, 14 Nov

13:30 –14:15 **KEYNOTE LECTURE**
Chair: Matias AUTIO, *Genome Institute of Singapore*

Age-Related Macular Degeneration: What goes wrong, how to fix it
Martin PERA, *The Jackson Laboratory, USA*

Session 7. Stem cell-based models for cardiac disease

Chair: Matias AUTIO, *Genome Institute of Singapore*

14:15 – 14:45 **Modelling cardiovascular-metabolic biology with iPS cells**
Roger FOO, *National University of Singapore*

14:45 – 15:15 **Matrix matters: Laminin-guided differentiation of cardiovascular progenitors from pluripotent stem cells**
Lynn YAP, *Nanyang Technological University, LKCM, Singapore*

15:15 – 15:45 AFTERNOON TEA BREAK

15:45 – 16:15 **Modelling acquired cardiac diseases with iPSCs: Insights from diabetic heart failure**
Chrishan RAMACHANDRA, *National Heart Research Institute, Singapore*

16:15 – 16:30 *Selected Abstract*
Mapping stress response-QTLs using iPSC-cardiomyocytes for heart failure
Brandon TAN, *National University of Singapore*

16:30 – 17:00 **Mitochondrial transplantation as a novel therapeutic strategy for cardiometabolic disorders**
Boon Seng SOH, *Institute of Molecular & Cell Biology, Singapore*

17:00 – 17:30 **AASCRM LECTURE – Australasian Society for Stem Cell Research**
Using iPSCs to model enteric nervous system development and for cell therapy
Lincon STAMP, *University of Melbourne, Australia & President ASSCR, Australia*

17:30 – 17:45 **AWARD PRESENTATION & CLOSING REMARKS**
Chair: Yun XIA, Nanyang Technological University, LKCM, Singapore

END OF DAY 3 - FAREWELL

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Applying the ISSCR Standards for Research

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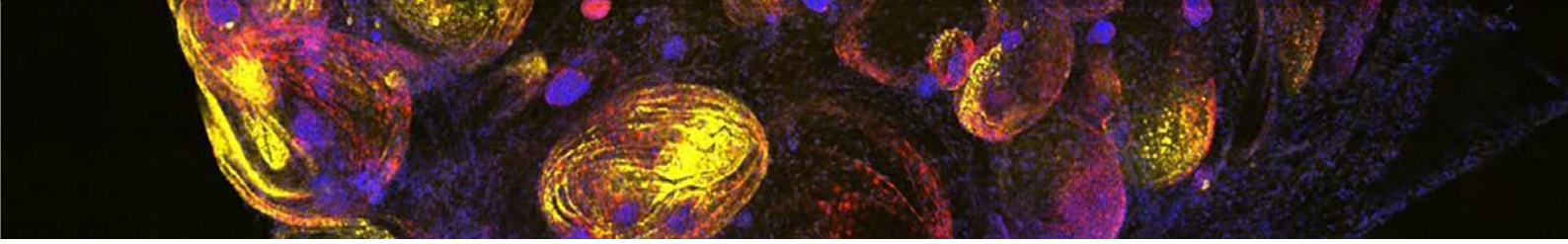
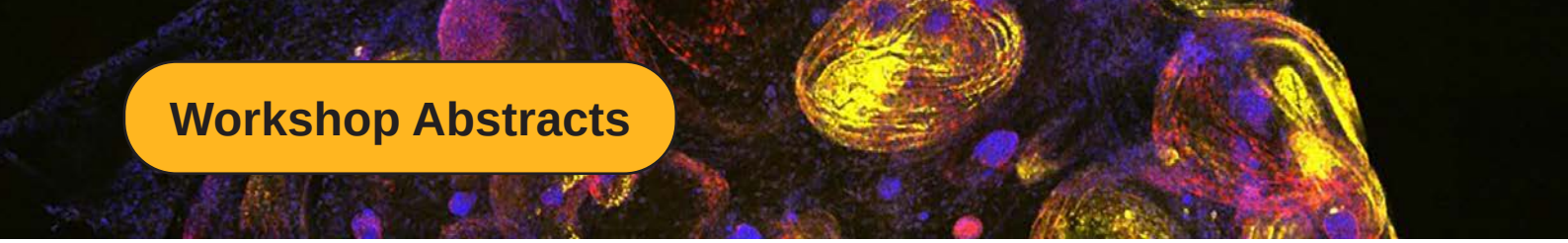


WORKSHOP SPEAKER ABSTRACTS

11 Nov 2025



Workshop Abstracts

Human pluripotent stem cells and the human embryo

Martin Pera

JAX Mammalian Genetics, The Jackson Laboratory, Bar Harbor, USA.

ABSTRACT

Pluripotency, the capacity to generate all tissues of the body, is a defining property of the epiblast – a transient cell population found in the pre- and post-implantation mammalian embryo. As development progresses through the peri-implantation period, the cells of the epiblast undergo dynamic transitions in pluripotency states concurrently with the specification of extraembryonic and embryonic lineages. In-depth study of heterogeneity in human PSC culture has revealed that cells grown under conventional conditions-sometimes referred to as primed pluripotent cells-exist in a continuum of epiblast states that spans a developmental timeframe from the early post-implantation state through to a stage just prior to gastrulation. The distribution of cells along this continuum varies from one cell line to another in a genetically determined fashion. We discuss the implications of these findings for the applications of hPSC in research and for our understanding of how variations in the Waddington landscape might affect resilience to disease in later life.

BIO

Martin Pera is a Professor at the Jackson Laboratory. Pera's research focus is the cell biology of human pluripotent stem cells. His laboratory at Monash University was the second in the world to isolate embryonic stem cells from the human blastocyst, and the first to describe their differentiation into somatic cells in vitro. Pera was amongst the first to analyze heterogeneity in human pluripotent stem cell cultures, work that has clarified the embryological coordinates of these cells and is critical to their use as models for human development. His research on neural differentiation of human pluripotent stem cells helped lead to the development of a new treatment for macular degeneration, a common form of blindness, now in clinical trial in Israel and California. At the Jackson Laboratory, he is using human stem cells to study the genetics of age-related macular degeneration and to develop new approaches to cell therapy of the disease.

iPSC & reprogramming

Jonathan Yuin Han Loh

Institute of Molecular & Cell Biology, Singapore & President SCSS

ABSTRACT

This presentation discusses the evolution of cellular reprogramming, highlighting how somatic cells can be converted into pluripotent or more potent states through methods like SCNT and transcription factor-driven iPSC generation. It traces the historical development from early models like Waddington's epigenetic landscape to landmark discoveries such as Gurdon's nuclear transfer experiments and Yamanaka's identification of four key factors for inducing pluripotency. The talk also covers recent advancements in reprogramming efficiency, including chemical methods and genome editing, and explores the potential therapeutic implications of these technologies in regenerative medicine.

BIO

Yuin-Han Jonathan Loh is the Deputy Executive Director and Research Director at the A*STAR Institute of Molecular and Cell Biology (IMCB. In addition, he is a Professor (Adjunct) at the National University of Singapore (NUS) Yong Loo Lin School of Medicine and a faculty member of the NUS Graduate School of Integrative Sciences and Engineering. Jonathan graduated with First Class Honours in Molecular Biology from NUS and completed his PhD in Integrative Sciences and Engineering at the NUS Graduate School, supported by the A*STAR Scholarship, where he earned the Philip Yeo Prize for the best paper. He furthered his training with a Postdoctoral Fellowship in Hematology and Oncology at Harvard Medical School and Boston Children's Hospital. His current research focuses on understanding the mechanisms that regulate cell fate changes, particularly how: 1) epigenetic factors interact with regulatory elements to coordinate gene expression; 2) transcription factors drive transdifferentiation and somatic cell reprogramming; and 3) epitranscriptomic regulation influences cell states. He is ranked by ScholarGPS among the top 0.07% of scientists globally in the field of stem cell research, based on quality metrics, with his publications cited over 24,240 times (Google Scholar) by peers worldwide. Jonathan's contributions have been recognized with several prestigious accolades, including the MIT TR35 Asia Pacific Award, Singapore Young Scientist Award, World Technology Network Fellowship, the Stem Cell Society Singapore Outstanding Investigator Award, Entrepreneurship World Cup and the ISSCR Public Service Award. He served as the President of the Stem Cell Society Singapore and as an executive council member of the Singapore Association for the Advancement of Science. Additionally, Jonathan founded two biotech start-ups, InnoCellular and Genovn, and is a board member of Nasdaq-listed Cytomed Therapeutics (GDTC).

Intestinal stem cells

Bon-Kyoung Koo

Center for Genome Engineering, Institute for Basic Science, Daejeon, S.Korea

BIO

Bon-Kyoung Koo is a mammalian geneticist studying E3 ubiquitin ligases—including Mib1 (Dev 2005, Neuron 2008), Rnf43 (Nature 2012, PNAS 2015), and Phf16 (Dev Cell 2024)—that regulate Notch, Wnt, and Hippo signaling in development, regeneration, and tumorigenesis. He revealed how signaling pathways are controlled by ubiquitin-mediated endocytosis and proteolysis, identifying Rnf43 and Znrf3 as tumor-suppressive membrane E3 ligases that degrade Wnt receptors via endo-lysosomal trafficking. He also defined key phosphorylation sites (Nat Commun 2020) and downstream mediators Daam1/2 (Sci Adv 2023), enabling their use in proteolysis-targeting antibodies (PROTABs). Dr. Koo pioneered genetic technologies—viral and BAC transgenesis, CRISPR/Cas9, and conditional knockouts—to establish adult stem cell-derived organoid systems (Nat Rev MCB 2020). His lineage-tracing studies defined Troy+ and isthmus gastric stem cells (Cell 2013; CSC 2019) and stem cell quiescence (CSC 2022). Recently, he developed mosaic genetics tools (Nature 2021; Nat Commun 2024) enabling fly-like genetic precision in mice.

Skeletal muscle stem cells

Reshma Taneja

Department of Physiology, National University of Singapore, Singapore

ABSTRACT

Skeletal muscle stem cells, also known as satellite cells, are essential for muscle growth, repair, and regeneration. Located between the basal lamina and sarcolemma of muscle fibers, these normally quiescent cells become activated in response to injury or stress. Once activated, they proliferate, differentiate into myoblasts, and fuse to repair or form new muscle fibers. Understanding skeletal muscle stem cells is crucial for advancing therapies in muscular dystrophies, age-related muscle loss (sarcopenia), and sports injuries. We will discuss ways to enhance satellite cell function or deliver healthy satellite cells to affected areas to improve muscle repair and restore strength. Addressing these challenges is essential for developing safe and effective satellite cell-based treatments for muscle disorders.

BIO

Reshma Taneja got her Ph.D. degree from the Indian Institute of Science and did her postdoctoral training in the laboratory of Prof Pierre Chambon, in France. She started her own laboratory at the Mount Sinai School of Medicine in New York City and moved to Singapore in 2008. She is currently Head of the Department of Physiology at the National University of Singapore. Her research program focuses on understanding how skeletal muscle is made, and how it is altered in muscle disorders such as muscular dystrophies, as well as in cancer (rhabdomyosarcoma). She has several received awards at NUS including the Faculty Research Excellence Award; Faculty Teaching Excellence Award; NGS Teaching Commendation Award; and the Graduate Mentor of the Year Award.

Neural stem cells & organoids

Alfred Sun

Duke-NUS Medical School, Singapore

BIO

A native of Hang Zhou, China, **Alfred Sun** came to Singapore in 1997 and completed his high school before taking up the A*STAR NSS-PhD scholarship. He obtained B.S. from Duke University and Ph.D from Stanford University under the supervision of Dr. Gerald Crabtree. He then returned to A'STAR, Singapore and joined Prof. Bing Lim's and later Prof. Ng Huck-Hui's lab as a postdoc. Prior to starting his own lab in Duke-NUS, Alfred was a junior PI in the National Neuroscience Institute. Alfred is currently leading an independent team using human neural cells to study neurodegeneration, particularly on Parkinson's.

Two roads to lineage specification: Direct differentiation and transdifferentiation

Yun Xia

Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore & ExCo SCSS

ABSTRACT

Precise control of cell fate is fundamental for modeling human development, understanding disease mechanisms, and enabling regenerative medicine. Achieving desired lineages can be realized through direct differentiation, which guides pluripotent stem cells along developmental trajectories using stepwise cues, or transdifferentiation, which converts one somatic cell type directly into another without passing through pluripotency. Direct differentiation offers developmental fidelity and scalability but often yields immature phenotypes. In contrast, transdifferentiation can bypass developmental barriers and preserve age-related features, though reprogramming efficiency and stability remain challenges. Integrating advances in transcription factor programming, epigenetic modulation, and microenvironmental engineering is progressively refining both strategies. Ultimately, combining these approaches may enable the generation of fully functional, patient-specific cell types for disease modeling, drug discovery, and tissue replacement, paving the way toward personalized regenerative therapies that faithfully recapitulate human biology and restore organ function.

BIO

Yun Xia is a Nanyang Assistant Professor and Provost's Chair in Stem Cell Biology at the Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore. Her research focuses on developing human stem cell-based models to study kidney development and disease. Dr. Xia's laboratory leverages direct differentiation and multicellular self-organization to generate kidney organoids that recapitulate the key structural and functional properties of the native organ. In recognition of her contributions to kidney organoid research, Dr. Xia received the SCSS Dr. Susan Lim Award for Young Investigator from the Stem Cell Society Singapore in 2020 and was selected to join the EMBO Global Investigator Network in 2021. Since 2022, she has served as an Associate Editor for Kidney International.

Paving the way for cGMP cell therapy manufacturing: process development and regulatory considerations

Jaichandran Sivalingam

Process Accelerator for Cell Therapy Manufacturing (PACTMAN), Bioprocessing Technology Institute, Agency for Science Technology & Research, Singapore

ABSTRACT

Cell and Gene therapy pipelines for regenerative medicine and cancer immunotherapy are actively being investigated for clinical use. To date, there are over 44 FDA approved cell and gene therapy products commercially available, and the list continues to grow. The cell therapy ecosystem in Asia and Singapore is actively evolving, with efforts in multiple areas such as developing more efficient and cost-effective manufacturing workflows for autologous CAR-T, developing scalable allogeneic manufacturing workflows for iPSC differentiated cells and allogeneic CAR-T, NK, gamma-delta T cells, among others. The Process Accelerator for Cell Therapy Manufacturing (PACTMAN) is a 3-year program that partners BTI (A*STAR) with Advanced Cell Therapy Research Institute, Singapore (ACTRIS) to provide support with pre-GMP process and analytical development to de-risk the path towards cGMP manufacturing. In this talk, I will touch on some of the critical process development and regulatory considerations for cGMP development of cell therapy manufacturing workflows.

BIO

Jaichandran Sivalingam (PhD), is a Principal Scientist and Group Leader for the Process Accelerator for Cell Therapy Manufacturing (PACTMAN) group at Bioprocessing Technology Institute, A*STAR (Singapore). A molecular biologist by training with over twenty years of research and industry experience in cell therapy development. He was previously involved in pre-clinical cell therapy pipeline development for Diabetes and Haemophilia A, at the National Cancer Centre, Singapore. Developed scalable manufacturing of induced pluripotent stem cells derived universal red blood cells for transfusion therapy at BTI (A*STAR). He was part of the Process, Science and Technology (PSAT) team involved in CAR-T pipeline development at Tessa Therapeutics, formerly a late-stage clinical company involved in immune-oncology pipeline development. He currently leads the PACTMAN group, A*STAR's cell and gene therapy initiative, to provide pre-GMP Process and Analytical Development support for cell therapy asset developers.

Stem cell clinical trials

Eng Soo Yap

National University Hospital (NUH) & Advanced Cell Therapy and Research Institute Singapore (ACTRIS), Singapore

ABSTRACT

Stem cell therapies are moving rapidly from bench to bedside, with applications spanning oncology, neurology, cardiology, autoimmune disorders, orthopedics, diabetes, and ocular disease. Globally, thousands of clinical trials are ongoing, and several therapies such as for graft-versus-host disease, Crohn's fistulas, and corneal burns have already received regulatory approval. In Singapore, with our robust regulatory framework, ethical oversight, and strong translational ecosystem have positioned the nation as a regional leader in regenerative medicine. This talk aims to provide an integrated overview of global and local trends, mechanisms of action, and the evolving industry landscape, equipping scientists and clinicians with insights into how stem cell research is shaping the next generation of therapies.

BIO

Eng Soo Yap is a clinical haematologist at the National University Hospital (NUH) and Ng Teng Fong General Hospital (NTFGH). He is Head of Department, Laboratory Medicine NTFGH and adjunct Associate Professor at the National University of Singapore. Beyond his clinical and academic roles, Dr Yap is the Chief Medical Officer at the Advanced Cell Therapy and Research Institute Singapore (ACTRIS), where he oversees product quality, regulatory compliance, and operational readiness for cGMP cell manufacturing. His work bridges frontline patient care, cGMP operations, and the translation of advanced cellular therapies into practice.

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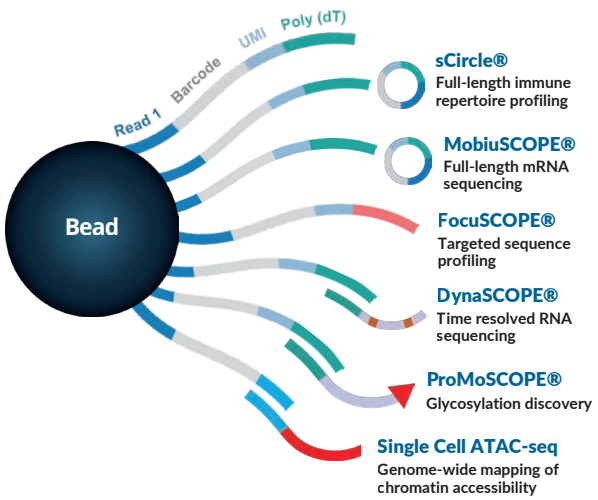

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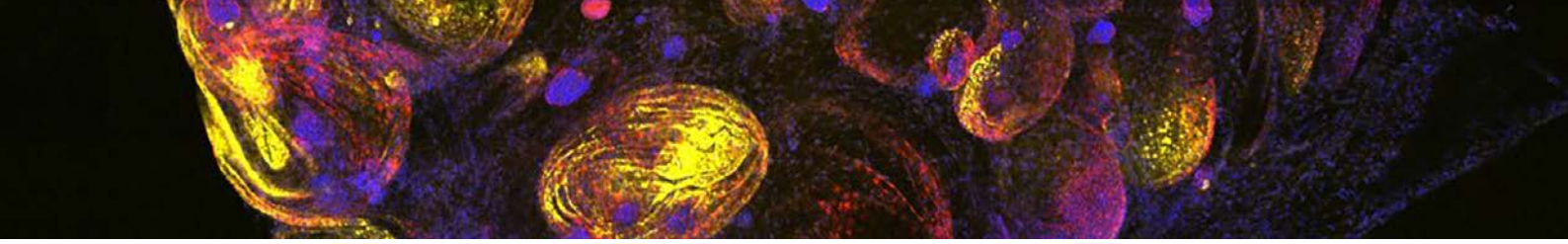


SPEAKER ABSTRACTS

Day 1

12 Nov 2025

Peripheral hematopoietic intervention to rescue neurodegeneration in the brain

Helen S Goodridge

Board of Governors Regenerative Medicine Institute, Cedars-Sinai Medical Center, Los Angeles, USA

ABSTRACT

Hematopoietic aging has a profound impact on the function of organs throughout the body, including the brain, where peripheral hematopoietic aging as well as local inflammatory responses impact cognitive function. We previously demonstrated that young bone marrow transplantation rescues cognitive decline in old mice, with reduced neuroinflammation and more synaptic connections in the hippocampus of young bone marrow recipients. Similarly, we recently demonstrated that injection of induced pluripotent stem cell-derived mononuclear phagocytes into the circulation reduces neuroinflammation, restores neuronal health and improves cognitive function in models of aging and Alzheimer's disease. Consistent with plasma transfer studies, the rejuvenating effects of these peripheral hematopoietic interventions appear to be a consequence of changes in the periphery rather than entry of transplanted cells into the brain. In ongoing studies, we are continuing to define the underlying mechanisms and exploring the potential for peripheral hematopoietic interventions to treat neurodegenerative diseases in humans.

BIO

Helen Goodridge, PhD is a Professor of Biomedical Sciences (Immunology) and Medicine (Hematology) and Associate Director of the Board of Governors Regenerative Medicine Institute at Cedars-Sinai Medical Center in Los Angeles. Her research focuses on the production and functional heterogeneity of monocytes and macrophages in the context of infection, cancer, healthy aging, and neurodegenerative diseases. In recent years, she has developed a key interest in neurodegeneration during healthy aging and Alzheimer's Disease through collaborations with Clive Svendsen PhD and others. Her lab aims to develop therapeutic strategies for neurodegenerative diseases, including immune cell therapies and rejuvenation of endogenous hematopoietic stem cells and/or their bone marrow niche.

Functional genomics of diabetes using hPSC-derived islet-like cells

Adrian Kee Keong Teo[1,2,3,4]

*[1]Stem Cells and Diabetes Laboratory, Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore; [2]Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [3]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [4]Precision Medicine Translational Research Programme (TRP), Yong Loo Lin School of Medicine, National University of Singapore, Singapore*

ABSTRACT

Diabetes is a debilitating chronic disease that is spiralling out of control, affecting more than 500 million people worldwide. Fundamentally, the progressive failure of pancreatic beta cells results in decreased insulin secretion, ultimately giving rise to hyperglycaemia and overt diabetes. In the past decade, donor- and patient-derived human induced pluripotent stem cells (hiPSCs) coupled with an ability to differentiate them into pancreatic islet-like organoids in fully-suspension cultures now provide an invaluable opportunity to study human beta cell failure in vitro. We have been contributing to the field by generating hiPSCs from monogenic and type 2 diabetes donors, followed by comprehensive diabetes disease modelling. Here, I will highlight our decade of efforts in using diabetes patient-specific hiPSC-derived pancreatic islet-like organoids harbouring defined gene mutations or variants to study human diabetes disease mechanisms, from monogenic diabetes to type 2 diabetes, actively contributing toward functional genomics of diabetes.

BIO

Adrian TEO obtained his B.Sc. (1st Class) from the National University of Singapore (NUS). He completed his Ph.D. on stem cell biology with Prof Ludovic Vallier at the University of Cambridge, under an A*STAR Scholarship. Concurrently, he was also an Honorary Cambridge Commonwealth Trust Scholar. He then trained with Prof Rohit Kulkarni at Joslin Diabetes Center, Harvard Medical School, as a Juvenile Diabetes Research Foundation (JDRF) fellow, on pancreatic islet biology and diabetes. Adrian is currently a Senior Principal Investigator at the Institute of Molecular and Cell Biology (IMCB), A*STAR; Division Director of the Cell and Molecular Therapy (CMT) Division at IMCB, A*STAR; a tenured Associate Professor at Yong Loo Lin School of Medicine, National University of Singapore; and Director of Graduate Affairs (DGA) of the Biomedical Research Council (BMRC), A*STAR. His laboratory uses human pluripotent stem cells for disease modelling of diabetes, developing therapeutics and cell therapy. He is also a co-founder of BetaLife Pte Ltd focused on the use of stem cell therapy for diabetes patients. He is a member of the Oxbridge Society of Singapore, the International Society for Stem Cell Research (ISSCR) and an EXCO member/Vice-Secretary of the Stem Cell Society Singapore (SCSS).

AASCRM LECTURE – Chinese Society for Stem Cell Research

In utero stem cell transplantation: From functional characterisation to disease modelling and therapeutic exploration

Fanyi Zeng

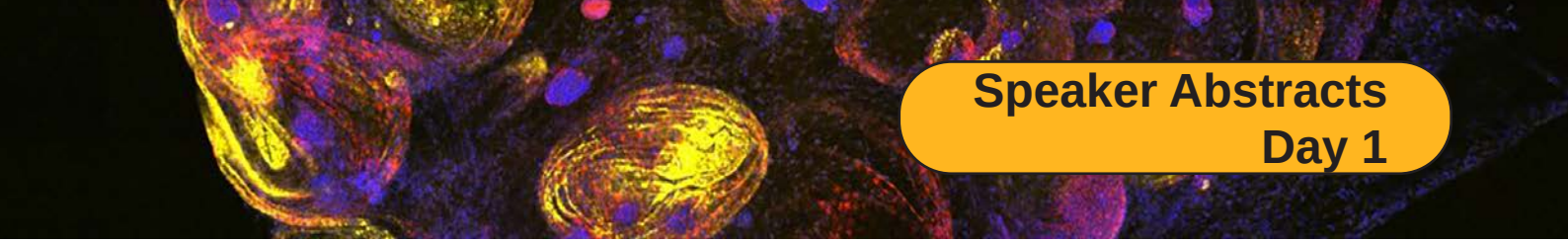
Department of Histo-Embryology, Genetics and Developmental Biology, Shanghai Jiao Tong University School of Medicine, China; Shanghai Institute of Medical Genetics, Shanghai Children's Hospital, Shanghai Jiao Tong University School of Medicine, China; NHC Key Laboratory of Medical Embryogenesis and Developmental Molecular Biology, Shanghai Key Laboratory of Embryo and Reproduction Engineering, China; School of Pharmacy, Macau University of Science and Technology, China

ABSTRACT

In utero stem cell transplantation (IUSCT) offers a unique approach to study stem cell engraftment, lineage differentiation under physiological conditions. Our work systematically explored the cell biology and therapeutic potential of transplanted stem cells across species and disease contexts. We generated a human-goat xenotransplant model and demonstrated long-term in vivo survival, proliferation, and differentiation of donor stem cells following IUSCT. We also developed a chronic myeloid leukemia (CML) animal model to characterize disease-related hematopoietic dynamics and validate donor cell integration in pathological conditions. Furthermore, using β^{654}-thalassemia mice as a genetic disease model, we achieved significant hematologic and phenotypic correction through in utero transplantation of hematopoietic stem/progenitor cells. Together, these results delineate the scientific progression from functional characterization to disease modeling and finally to preclinical therapy, highlighting IUSCT as a promising platform for prenatal gene and cell-based interventions.

BIO

Fanyi Zeng, an MD-PhD graduate of the University of Pennsylvania Perelman School of Medicine, is a Distinguished Professor at Shanghai Jiao Tong University and Director of Shanghai Institute of Medical Genetics. Her distinguished honors include being a Changjiang Scholar, a chief scientist of China's 973 Program, and an Academic Advisory Committee Fellow of the Chinese Academy of Medical Sciences. Her research integrates human genetics, developmental biology, and stem cells to advance the diagnosis and treatment of genetic diseases. She has been recognized with awards including second prize of National Prize for Natural Sciences, first prize of Natural Science Award of the Ministry of Education, and inaugural Young Women Scientist Award from TWOWS. Professor Zeng also holds key leadership roles, including Chair of the Human and Medical Genetics Committee of the Genetics Society of China and Vice President of the Chinese Society for Stem Cell Research.



Abstract selected talk

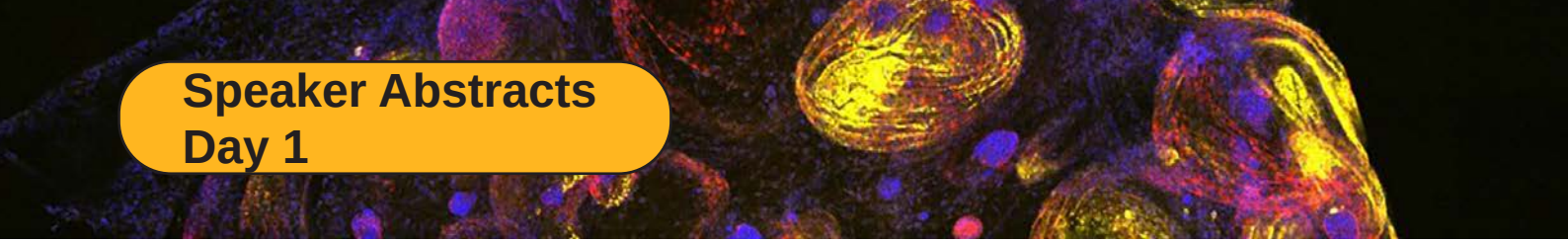
Induced macrophage-kidney organoids unravel context-dependent immune modulation in kidney development and disease

Huaming Wang, Meng Liu, Chao Zhang, Tian Zhang Yun Xia

Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

ABSTRACT

Macrophages are a major component of the human kidney's immune landscape, yet typical kidney organoid models lack these resident immune cells. To fill this gap, we created an immune-competent kidney organoid system by deriving macrophages and kidney organoids from the same pluripotent stem cell line and integrating the macrophages into the organoids. We discovered that macrophages incorporated early into developing organoids became long-term residents with tissue-specific phenotypes, including the expression of kidney macrophage markers. These resident macrophages actively supported tubular epithelial repair after acute injury, illustrating their protective function. In contrast, kidney organoids derived from polycystic kidney disease patient iPSCs produced a pathogenic environment rich in inflammatory cues. Monocytes added to these organoids migrated into the tissue and differentiated into M2b-like macrophages, which promoted cyst formation and inflammation, aggravating the disease phenotype. Our induced macrophage–kidney organoid platform therefore recapitulates both homeostatic and pathogenic interactions between macrophages and kidney tissue. This system offers a versatile tool for investigating macrophage biology in human kidney development, injury repair, and disease progression, and it may enable immunomodulatory therapies in a human-relevant context. Additionally, this system can be adapted to model other kidney diseases and to investigate macrophage differentiation and function across diverse disease contexts.



Speaker Abstracts Day 1

Abstract selected talk

Hypoimmunogenic retinal pigment epithelial cells promote immune tolerance for off-the-shelf retinal regenerative therapy

Asfa Alli-Shaik[1], Bhav Harshad Parikh[1,2], Zengping Liu[1,2,3], Fritz Lai[1], Regha Kakkad[2], Qi-Jing Li[1], Qingfeng Chen[1,5], Kah-Leong Lim[4,6], Xinyi Su[1,2,3]

[1]Institute of Molecular and Cell Biology, Agency for Science, Technology and Research, Singapore, [2]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [3]Singapore Eye Research Institute, Singapore, [4]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, [5]Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, [6]Department of Research, National Neuroscience Institute, Singapore

ABSTRACT

Age-related macular degeneration (AMD) is a leading cause of vision loss in the elderly, affecting over 200 million people worldwide. In advanced AMD, where retinal pigment epithelial (RPE) cell death leads to irreversible central vision loss, stem cell-derived RPE transplantation holds therapeutic potential; however, its success remains limited by low efficacy and immune rejection. Here, we report the application of human umbilical cord lining epithelial cells (CLECs)-derived iPS (termed “CLiPS”) as a genetically unmodified, naturally occurring, hypoimmunogenic cell source for retinal cell therapy. CLiPS-derived RPE allografts exhibited a reduced generalized systemic and localized immune response in humanized mice. Single-cell transcriptome of CLiPS-RPE grafts in comparison with other stem cell-derived grafts in humanized mice, revealed a unique microenvironment dominated by T-regulatory cells (Tregs) and immunosuppressive myeloid populations. CLiPS-RPE also elicited minimal activation of allo-rejection signature upon transplant with persistent low major histocompatibility complex (MHC) gene expression. Single cell transcriptome of subretinal CLiPS-RPE explants in rabbits, in the absence of immunosuppression, confirmed high functional maturity of CLiPS-RPE, together with low MHC expression and enhanced immune-tolerant signatures. Overall, our results demonstrate that the intrinsic hypoimmunogenicity of CLiPS promotes an immune-tolerant microenvironment, positioning CLiPS as a universal cell source for “off-the-shelf” allogeneic cell therapies.

Corneal endothelial cell therapy: Current practise

Jodhbir Mehta

Singapore National Eye Centre, Singapore Eye Research Institute, Duke-NUS

ABSTRACT

Corneal Transplantation is the leading tissue transplant procedure in the world. The most common part of the cornea that is replaced is the corneal endothelium. In the last two decades we have seen a significant shift from whole corneal transplantation to selective tissue transplantation, of the diseased endothelium. This has led to a significant improvement in outcomes with respect to visual acuity, and lower rates of graft rejection. However, despite this, there is still a reliance on donor cadaver tissue. In addition, between 20-30% of all tissue that is harvested from eyebanks cannot be used for endothelial surgery due to low endothelial cell counts. To counteract this issue, disruptive technology in the form of cell-based therapies has come to the forefront. There are currently 4 clinical trial running 3 with cadaver-based cell expansion, 1 from iPSC. In addition a non-cultured novel endothelial cell therapy is also undergoing clinical trial. The talk will give an update on the current state of these trials.

BIO

Jodhbir Mehta is the Deputy Medical Director (Research), Distinguished Professor in Clinical Innovation in Ophthalmology at the Singapore National Eye Centre (SNEC), and Academic Vice-Chair (Research) at SingHealth Duke-NUS. He is also Executive Director and co-head of the Regenerative Therapy and Cataract & Refractive Research Group at SERI, Senior Consultant, and former Head of the Cornea and External Eye Disease Department at SNEC. He has published over 540 peer-reviewed papers, 24 book chapters, with H-index of 81 and over 24,000 citations. He has delivered >350 invited lectures and received 79 prestigious awards (20 Named Lectures). He has been recognized as one of the most influential people in the world of ophthalmology both by featuring in the Ophthalmologist's Power List, Asia-Pacific Power List and also the top 2% of scientist in Ophthalmology by Elsevier. He holds 24 patents (6 commercialized and licensed to companies) and has trained 30 international fellows, 5 masters, and 8 PhD students. His research focuses on corneal transplantation, laser technology, imaging, infections, refractive surgery, keratoprosthesis, and genetics. Prof Mehta is also an active member of APAO and other Asia-Pacific professional societies. He currently is the Vice-President of International Relations of the American Cornea Society.

Speaker Abstracts Day 1

Effective targeted transgene knock in & expression in hPSCs

Matias I Autio

*Genome Institute of Singapore, A*Star, Singapore; Cardiovascular Research Institute, YLL School of Medicine, National University of Singapore, Singapore*

ABSTRACT

Stable expression of transgenes is essential in both therapeutic and research applications. Traditionally, transgene integration has been accomplished via viral vectors in a semi-random fashion, but with inherent integration site biases linked to the type of virus used. The randomly integrated transgenes may undergo silencing and can also lead to dysregulation of endogenous genes. Genomic safe harbour (GSH) loci have been proposed as safe sites in the human genome for transgene integration. Although several sites have been proposed for transgene integration, most of these do not meet criteria set out for a GSH and or have not been characterised extensively. We conducted a computational analysis to identify 25 unique putative GSH loci in active chromosomal compartments. We validated stable transgene expression and minimal disruption of the native transcriptome in three GSH sites *in vitro* using human embryonic stem cells (hESCs) and their differentiated progeny. Furthermore, for easy targeted transgene expression, we have engineered landing pad expression cassettes into the three validated GSH in hESCs and induced pluripotent stem cells. For high efficiency integration of transgenes, we optimised the Bxb1-recombinase and other reagents to reach up to 50% targeted integration of a payload without selection. The generated landing pad hPSC lines and recombination reagents allow for quick and easy targeted expression of genes of interest in the pluripotent cell state or in cells differentiated to the cell type of interest.

BIO

Matias I Autio did his undergraduate and postgraduate studies at Imperial College London. In 2013 he joined the group of Prof Roger Foo in the Genome Institute of Singapore as a post-doctoral fellow working on genome engineering of stem cell models for cardiovascular disease. He is currently a Senior Scientist in the Genome Institute of Singapore and a Senior Research Fellow in the National University of Singapore and works on genome engineering of human pluripotent stem cell lines and other cell types for cell and gene therapy applications.

Microphysiological systems: Development of vascularized tumor models for immunotherapy

Geetika Sahni

AIM BIOTECH Pte Ltd, Singapore

ABSTRACT

The presented work centres on the creation of vascularized tumoroid models—an advanced microphysiological system (MPS) focused to transform cancer research and immunotherapy development. We integrate AIM Biotech's MPS platform for organoids and biopsies, organiX, and all-in-one vascularization kit, VasQ Kit with Thermo Fisher's well-characterized patient-derived tumoroid cell lines, to generate the model. The focus of the work is to drive innovation and accelerate progress across the wider field of drug discovery and development.

BIO

Geetika Sahni is an Application Development Scientist at AIM Biotech.

iPSC-iNK workflow solutions for scalable cell therapy manufacturing

Ryan Lim

Thermo Fisher Scientific, Bioscience Division, Cell Gene and Advanced Therapy, Asia Pacific and Japan

ABSTRACT

Induced pluripotent stem cell-derived natural killer (iPSC-iNK) therapies are redefining the future of allogeneic immunotherapy. Thermo Fisher Scientific accelerates this journey with scalable, closed, and automated workflow solutions spanning iPSC generation, expansion, formulation, fill, and finish. Our end-to-end platform—featuring Gibco™ Cell Therapy Systems (CTS™) reagents and platforms—streamlines manufacturing, reduces costs, and drives consistency from research to clinic. Designed for regulatory confidence and commercial scalability, these solutions focus on derisking the process while maximizing efficiency and yield. Backed by Thermo Fisher's global expertise and trusted technologies, our expanding portfolio will soon introduce next-generation innovations to further simplify and scale iPSC-iNK manufacturing—empowering developers to deliver transformative therapies faster, safer, and more affordably.

BIO

Ryan Lim is a Business Development Manager with Thermo Fisher supporting the Cell, Gene and Advanced Therapy portfolio across the Asia Pacific and Japan region. His primary role is to establish longer-term partnerships and collaborations with clients in this space while supporting their current needs to develop their new and existing pipelines. Prior to this role, he was the technical specialist and field application scientist for both the Cell & Gene Therapy and Immunoassay portfolios. As such, his focus was on providing technical support for multiple products, as well as integrated workflow solutions, to researchers and organisations in the Asia Pacific and Japan region. Allowing them to utilise the latest solution effectively, thereby accelerating their work and overcoming their roadblocks.

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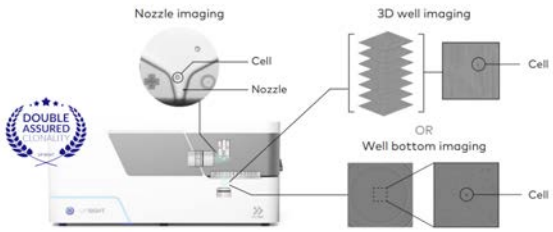

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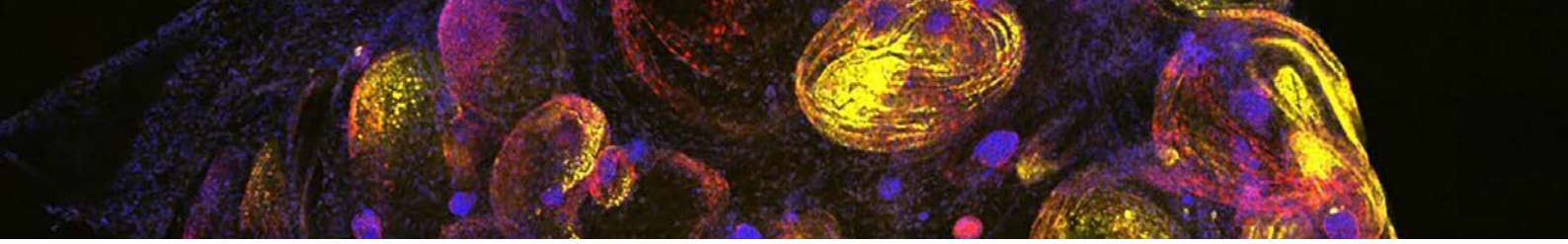
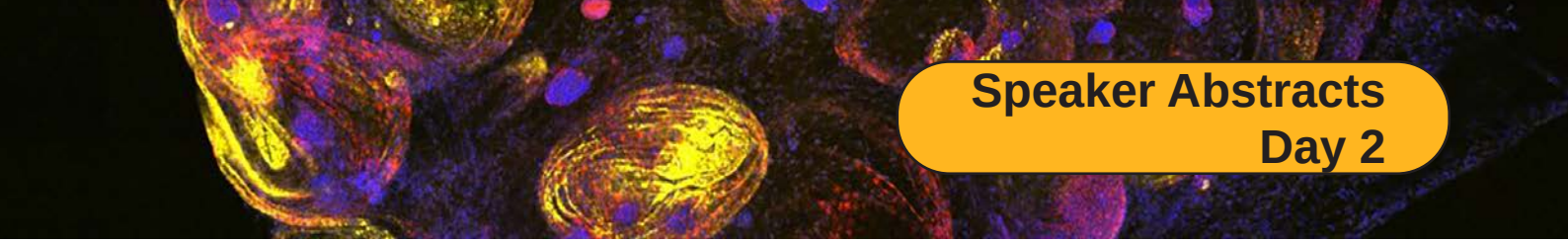


SPEAKER ABSTRACTS

Day 2

13 Nov 2025



Speaker Abstracts Day 2

KEYNOTE LECTURE

Sall4 dependent chromocenter remodeling and cell fate control

Duanqing Pei

Regenerative Biology, School of Life Sciences, Westlake University, China

ABSTRACT

The interaction framework between key transcription factors (TFs) and chromocenters (CCs) is vital for cell fate control. CCs are heterochromatin islands, TFs serve as shuttle boats to silence or activate gene expression by transport specific chromatin region to approach or depart CCs aggregates, which should be regulated by up-stream signals. Here we show that SALL4, a classic TF possesses transcriptional activation and repression function, can form shell condensates (SCs) around CCs aggregates under high resolution light microscope, the collaboration between them is important for somatic cell reprogramming and ESCs fate maintenance. Nevertheless, BMP4-DUSP9 axis disrupts SALL4 SCs-CCs structure by pT903-dephosphorylation. Here we described a novel structure of SALL4-CCs, clarified pT903 is necessary for SALL4 SCs-CCs interaction and cell fate control, established the correlation between DUSP9 catalytic activity and SALL4pT903. This work provided direct evidence upon TFs-PP-CCs collaboration and cell fate determination.

BIO

Duanqing Pei is Chair Professor of Regenerative Biology at School of Life Sciences, Westlake University. Dr. Pei received his PhD from the University of Pennsylvania in 1991; trained as a postdoctoral fellow at University of Michigan from 1991 to 1996. Dr. Pei's primary interest is to understand cell fate control. His lab pioneered cellular reprograming and discovered: 1) Vitamin C as an epigenetic regulator that enhances cellular reprograming through histone and DNA demethylations; 2) Epithelial to mesenchymal (EMT) and mesenchymal to epithelial (MET) transitions as drivers for iPSC generation; 3) Urine epithelial cells as a source of stating cells for reprograming. He has proposed a chromatin open-close binary logic for cell fate control and an conceptual interface between pluripotent and somatic states. These concepts are still driving current works in the lab. Dr. Pei won national natural science award twice and the distinguished achievement medal from Chinese Academy of Sciences. He is EMBO Associate Member and MAE (Member of Academia Europa).

Indispensable role of ERK signal in the self-renewal and differentiation of embryonic stem cells

Xiaowei Duan, Shanshan Nai, Lingyi Chen

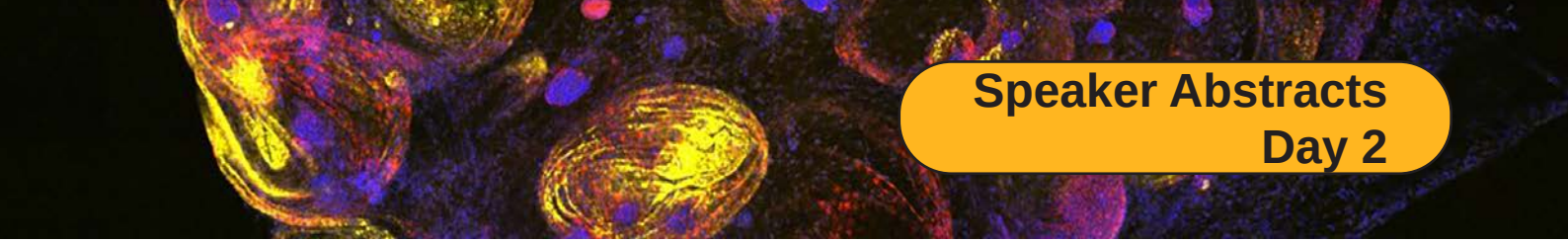
Department of Genetics and Cell Biology, College of Life Sciences, Nankai University, China

ABSTRACT

Inhibition of MEK/ERK signaling by pharmacological MEK inhibitor promotes self-renewal and pluripotency of mouse embryonic stem cells (ESCs). In contrast, knockout of Erk leads to rapid telomere shortening and genomic instability, in association with mis-regulated expression of pluripotency genes, reduced cell proliferation, G1 cell cycle arrest, and increased apoptosis, implying a dual role of ERK signaling in the self-renewal of ESCs. Here, we revealed that ERK regulates the self-renewal and differentiation of ESCs, as well as the telomere length, through phosphorylating its downstream targets, including DDX3X, HNRNPF and ESRRB.

BIO

Lingyi Chen obtained a BS degree in Biochemistry and Molecular Biology from Peking University, Beijing, China, in 1999, and a PhD degree in Biology from Northwestern University, Evanston, Illinois, the United States in 2004. After completing his postdoctoral training at Harvard University from 2005 to 2008, he moved back to China and set up his laboratory at Nankai University, Tianjin, in 2008. He is currently a Professor of Cell Biology in the College of Life Sciences. His laboratory is interested in molecular mechanisms underlying mouse preimplantation development and pluripotency maintenance in embryonic stem cells (ESCs). His group has made important discoveries about the function and molecular mechanisms of MEK/ERK signaling pathway in ESCs, including demonstrating the indispensable role of ERK in the self-renewal of ESCs, and revealing the ERK-independent function of MEK.



Speaker Abstracts Day 2

Abstract selected talk

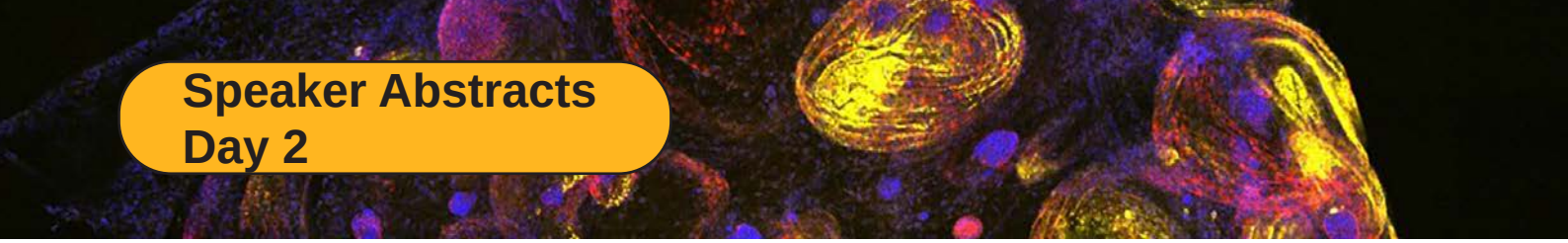
Single-cell m6A atlas decodes dynamic epitranscriptomic programs that orchestrate cell fates throughout development

Kiyofumi Hamashima[1]*, Ka Wai Wong[1,7], Jia Hao Jackie Teo[1,2,7], Reshma Taneja[2], Hu Li[3], Yuin-Han Loh[1,2,4,5,6]*

*[1]Cell Fate Engineering and Therapeutics Lab, Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore; [2]Department of Physiology, NUS Yong Loo Lin School of Medicine, Singapore; [3]Center for Individualized Medicine, Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, USA; [4]Department of Biological Sciences, National University of Singapore, Singapore; [5]NUS Graduate School's Integrative Sciences and Engineering Programme, National University of Singapore, Singapore; [6]Lead contact; [7]These authors contributed equally*

ABSTRACT

N⁶-methyladenosine (m⁶A) modification controls diverse cell fates during development. However, single-cell m⁶A profiling remains technically limited in complex, native tissues. To address this, we developed m6A-CT, a method that enables efficient in situ capture of m⁶A, compatible with droplet-based single-cell sequencing. We further refined this approach into m6A-CT2, which offers enhanced sensitivity and specificity, making it suitable for profiling primary tissues. Using m6A-CT2, we mapped the m⁶A landscape in over 280,000 cells from mouse post-implantation embryos at E7.5 to E12.5. This atlas reveals extensive m⁶A heterogeneity across 63 major cell types and dynamic m⁶A remodeling during lineage specification, refining high-resolution developmental trajectories. Our analysis identified numerous lineage-specific m⁶A regulators and targets, including transcription factors, signaling molecules, and transposable elements. Notably, we uncovered a cardiac lineage-specific m⁶A program regulated by the m6A eraser, which facilitates the metabolic transition to oxidative phosphorylation during maturation. Altogether, this study provides the first large-scale view of the epitranscriptomic landscape in development and reveals a regulatory layer beyond classical epigenetics.



Speaker Abstracts Day 2

Abstract selected talk

Decoding the genetic landscape of human evolution

Richard She

School of Biological Sciences, Nanyang Technological University, Singapore

ABSTRACT

The 3-fold expansion of the cerebral cortex is the defining feature of human evolution. This extraordinary transformation occurred over a remarkably short evolutionary time span of ~7 million years. However, the causal mechanisms and pathways that govern size control of the developing brain have not yet been systematically investigated. The focus of my research program will be to use comparative studies of humans and great apes to pinpoint the cellular and molecular principles that led to the emergence of our unique human features. Our approach draws inspiration from classical developmental genetics paradigms such as the Heidelberg screens, which identified many of the key signaling pathways that govern morphogenesis. However, while the core elements of these pathways are highly conserved from fruit flies to humans, unique aspects of human development arise from altered timing, regulation, and complexity. Performing parallel screens in closely related species allows us to identify key species differences in development. We plan to observe the balance of self-renewal and differentiation in neural progenitor cells, the key cell type that gives rise to virtually all neurons. By making perturbations to neuronal progenitor cells at genome-wide scale, we will systematically identify the key pathways that regulate human brain expansion.

Long-term expandable mouse and human chondroprogenitor cells achieve functional cartilage repair in vivo

Ronghui Li[1,2], Chengzhen Liang[1,3], Chao Yu[3], Zhongwei Li[1,4]

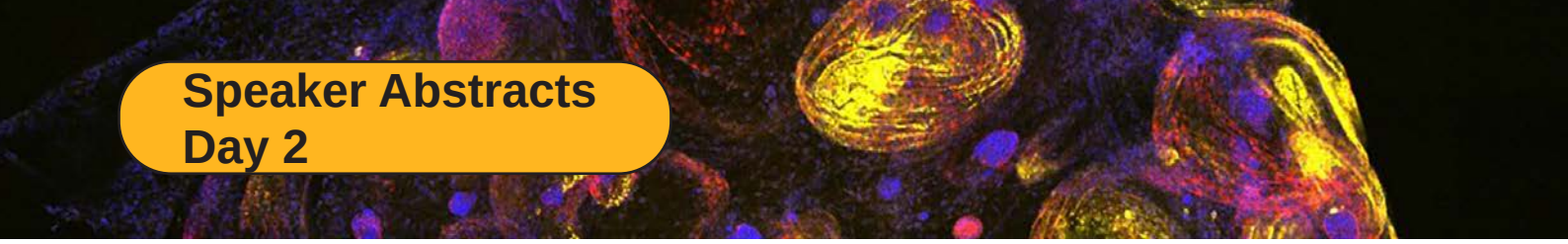
[1]Gene Expression Laboratory, Salk Institute for Biological Studies, USA; [2]NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI), National University of Singapore, Singapore, Singapore; [3]Department of Orthopedics, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, PR China; [4]Department of Stem Cell Biology and Regenerative Medicine, Keck School of Medicine, University of Southern California, USA

ABSTRACT

Chondroprogenitor cells (CPCs) in the limb bud are transient precursors that generate all chondrocytes during cartilage development, but their in vitro expansion and therapeutic potential remain unclear. To address this challenge, we isolated CPCs from mouse embryo and performed systematic screening to develop a robust expansion system. This system also supported long-term expansion of human CPCs isolated from appropriate embryonic stages or captured during hiPSC differentiation. Both mouse and human eCPCs demonstrated remarkable chondrogenic potential, differentiating into functional chondrocytes in vitroand forming hyaline cartilage-like structures. Single-cell RNA sequencing further validated the sustained progenitor identity of CPCs during prolonged expansion. Moreover, upon in vivo transplantation, eCPCs-derived chondrocytes successfully integrated with host cartilage tissue, synthesizing hyaline cartilage-specific extracellular matrix. Collectively, this study presents the first proof-of-concept that in vitro expandable CPCs can achieve functional cartilage repair in vivo and provide a versatile platform for studying chondrogenesis and modeling cartilage pathologies.

BIO

Ronghui Li is an Assistant Professor at the National University of Singapore and leads the SynDevBio Lab. He earned his Ph.D. in Cellular and Molecular Biology from the University of Wisconsin–Madison, where he studied the role of MeCP2 in neurodevelopmental disorders. Before joining NUS, he was a Scientist at Altos Labs and a Postdoctoral Fellow at the Salk Institute, focusing on stem cell differentiation, organoid development, and cellular rejuvenation. His research integrates synthetic biology, developmental biology, and bioengineering to engineer multicellular systems for regenerative medicine and disease modeling. With expertise in stem cell and 3D culture, gene editing, and organoid technologies, Ronghui aims to create innovative platforms for studying embryogenesis and developing therapies.



Speaker Abstracts Day 2

A novel mRNA-lipid nanoparticle platform to rapidly generate functional forebrain neurons from human pluripotent stem cells using NGN2

Robert Judson[1], Minoo Karmi1, Savitha Deshmuk[1], Eloi Mercier[1], Gary Braun[1], Charlotte Ellis[1], Mark Hills[1], Erin Knock[1], Allen C. Eaves[1,2], Sharon A. Louis[1], Arwen L. Hunter[1]

[1]STEMCELL Technologies Inc., Canada; [2]Terry Fox Laboratory, Canada

ABSTRACT

Differentiation of human pluripotent stem cells (hPSCs) into neuronal cell types has become a cornerstone of neurological research by providing unique cellular models of human diseases. While lentiviral delivery of the transcription factor neurogenin-2 (NGN2) is widely used to accelerate this process, it comes with challenges such as genomic integration risks, variability, and labor-intensive steps. To address these limitations we developed the STEMdiff™-TF Forebrain Induced Neuron Differentiation Kit, an integration-free system that simplifies the generation hPSC-derived neurons using mRNA-lipid nanoparticle (LNP) delivery of NGN2. This system enables rapid neuron differentiation, promotes functional maturation and sustains robust synaptic activity. Functional characterization confirms the generation of neurons with a glutamatergic forebrain subtype, which are also compatible with astrocyte co-culture. This technology provides a rapid, simple and user-friendly approach to generate hPSC-derived neurons and creates a robust platform to study human neurons.

BIO

Robert Judson is Associate Director of Pluripotent Stem Cell Biology at STEMCELL Technologies, where he leads efforts to develop innovative tools that advance stem cell research. He earned his PhD in Cell and Molecular Biology from the University of Aberdeen, Scotland, and completed postdoctoral training in Regenerative Medicine at the University of British Columbia, Canada. At STEMCELL, his current work focuses on mRNA-based strategies to precisely control lineage specification of human pluripotent stem cells, enabling applications in neuroscience, disease modeling, and regenerative medicine. With interests spanning molecular biology, synthetic biology, and developmental biology, Dr. Judson integrates mechanistic insight with translational innovation to accelerate discovery in stem cell biology and cell therapy. Outside the lab, he is an avid runner, backcountry skier, and chess enthusiast.

Single-cell multiomics identifies chromosome 21 regulators of intellectual disability genes in Down Syndrome

Michael Lattke[1], Wee Leng Tan[2], Salil Kalarikkal Sukumaran[2], Kagistia Hana Utami[2], Marcos Sintes[1,2], Srinivasan Sakthivel[2], Jonathan Tan[2], Auriel Lim[2], Bansal Aysha Vibhavari[2], Katerina Rekopoulou[3], Nik Matthews[3], Ivan Alic[4,5], Željka Krsnik[6], Dean Nizetic[4], Boaz P. Levi[7], Vincenzo De Paola[1,2]

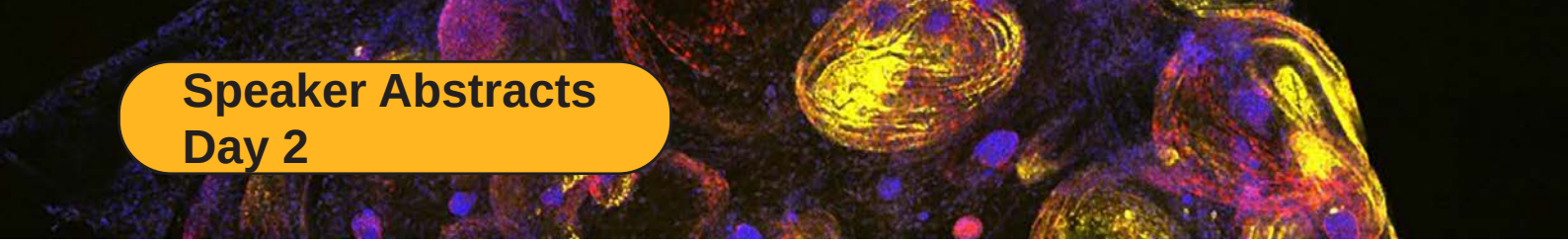
[1]Department of Brain Sciences, Faculty of Medicine, Imperial College London, UK; [2]Duke-NUS Medical School, Singapore; [3]NIHR Imperial BRC Genomics Facility, Imperial College London, UK; [4]The Blizard Institute, Faculty of Medicine and Dentistry, Queen Mary University of London, UK; [5]Department of Anatomy, Histology and Embryology, Faculty of Veterinary Medicine, University of Zagreb, Croatia; [6]Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Croatia; [7]Allen Institute for Brain ScienceUSA.

ABSTRACT

Down syndrome (DS), caused by an extra copy of chromosome 21, is the most common genetic cause of intellectual disability, affecting about 1 in 700 live births. Despite extensive research, it remains unclear how the increased dosage of ~200 genes on chromosome 21 disrupts cortical development, critical for higher cognitive functions. We generated a single-cell atlas of the human fetal cortex, capturing transcriptomic and chromatin landscapes during 11–20 weeks post-conception—a key window of cortical maturation. In parallel, we use iPSC-derived neurons and glia from individuals with DS to model human brain circuit formation and disease mechanisms. To overcome the limitations of conventional in vitro systems, we integrate iPSC-based models with xenotransplantation and multiomic analyses to investigate how trisomy 21 may drive cognitive impairment. This approach reveals molecular and cellular mechanisms of DS and highlights potential therapeutic targets for restoring neural circuit function.

BIO

Vincenzo De Paola received his Ph.D. in Neurobiology from the University of Basel, Switzerland, and completed an EMBO postdoctoral fellowship with Dr. Karel Svoboda at Cold Spring Harbor Laboratory, USA. He currently holds academic appointments at Imperial College London and Duke-NUS Medical School in Singapore. His research has uncovered fundamental mechanisms of synaptic plasticity and now focuses on developing advanced human in vivo models to elucidate the mechanisms of neural circuit dysfunction and to advance new therapeutic strategies for complex genetic disorders such as Down syndrome.



Speaker Abstracts Day 2

Decoding human neurodegeneration using stem cells

Rickie Patani

NUS Life Sciences Institute, Singapore

ABSTRACT

As a physician-scientist, I am passionately committed to understanding and ultimately curing devastating diseases. In particular, my laboratory studies diseases of the nervous system, focusing on motor neuron disease (ALS). In ALS, patients lose the ability to move, eat, speak and ultimately breathe. ALS is untreatable because we do not understand the underlying cause(s) of disease. In order to understand disease mechanisms, we use human stem cells generated from real patients. With over 15 years of experience using this technology, we can now transform stem cells from patients into human nerve cells and, separately, their support cells (called glia). This approach allows us to determine the sequence of disease-related events within particular cell types. This lecture will introduce the background clinical features of ALS before showcasing what our laboratory has contributed to the field. Our overarching goal is to identify precisely what goes wrong, when this begins and in which cell type. Broadly, I will cover how the following phenomena contribute to motor neuron degeneration in ALS: i) deregulated RNA metabolism; ii) reactive transformation of astrocytes. More specifically, I will focus how on a form of alternative splicing called intron retention is deregulated in ALS and may drive pathogenesis in different cell types. The more we understand about ALS using these approaches, the more precisely we will be able to target salient underlying disease mechanisms for ultimate patient benefit.

BIO

Rickie Patani is a Neurologist and Cell Biologist. He trained in Neurology in the UK including in UCL Queen Square and Addenbrooke's, Cambridge. He obtained a PhD and post-doctoral experience in Cambridge University and set up his lab at UCL Queen Square Institute of Neurology in 2013. He moved to the Francis Crick Institute in 2017. In 2018, Rickie was elected Fellow of the Royal College of Physicians (UK). He was appointed full Professor at UCL in 2019. Rickie recently left his role as a Senior Group Leader at the Francis Crick Institute as he was appointed Director of the Neurobiology Programme at NUS Life Sciences Institute and Professor of Neuroscience at NUS in the Departments of Medicine and Anatomy. Rickie was recently also elected Fellow of the Academy of Medical Sciences. Rickie's Lab is passionately committed to understanding neurodegenerative disorders in order to uncover new therapies. His team works primarily on the themes of RNA metabolism and cellular autonomy in ALS/FTD using human induced pluripotent stem cell models as a primary discovery platform.

Harnessing endothelial cell plasticity to restore tissue homeostasis

Christine Cheung

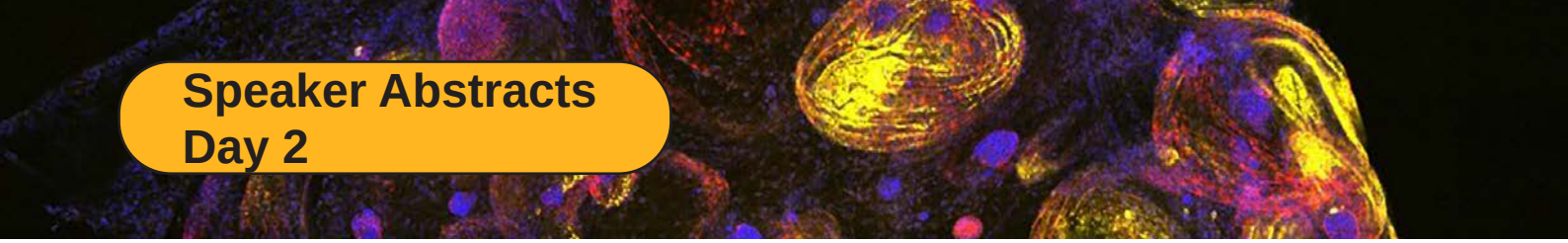
*[1]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; [2]Institute of Molecular and Cell Biology, A*STAR, Singapore*

ABSTRACT

Blood vessel dysfunction underlies the crux of many chronic and degenerative diseases. Vascular endothelial cells possess an inherent plasticity, enabling them to de-differentiate or transdifferentiate as part of normal tissue repair. However, our recent studies reveal that this plasticity becomes dysregulated in pathological contexts such as stroke, vascular dementia, and metabolic disorders. We show that endothelial cell de-differentiation is associated with gene programs involved in vascular development, embryonic patterning, and progenitor-like states, suggesting a reversion to a more immature phenotype. This aberrant reprogramming may contribute to maladaptive vascular remodeling triggered by sustained hypoxia and inflammation. Using mouse disease models and human pluripotent stem cell–derived arterial and venous cell subtypes, we have identified molecular drivers of this dysfunctional remodeling. In this talk, I will present key examples demonstrating how modulation of endothelial plasticity can restore vascular function, improving blood flow perfusion and re-establishing proper tissue zonation.

BIO

Christine Cheung is an Associate Professor of Vascular Biomedicine, the Assistant Dean (PhD Studies and Professional Development), and holds the Provost's Chair in Medicine at the Lee Kong Chian School of Medicine, Nanyang Technological University. She received her PhD in Cardiovascular and Stem Cell Medicine from the University of Cambridge and graduated with First Class Honors in BEng from Imperial College London. Her research in vascular disease biology has earned several recognitions. She was named a World Economic Forum Young Scientist in 2019 and an Honoree of the Ten Outstanding Young Persons of Singapore. Her awards include the HFSP Young Investigator Grant, L'Oréal Singapore For Women in Science Fellowship, and IMCB Independent Fellowship. She also received the Young Investigator Prize from the British Society for Cardiovascular Research and the Paul Dudley White International Scholar Award from the American Heart Association.



Speaker Abstracts Day 2

AASCRM LECTURE – Japanese Society for Regenerative Medicine

Strategic development of next-generation artificial platelets informed by reverse translational research

Koji Eto

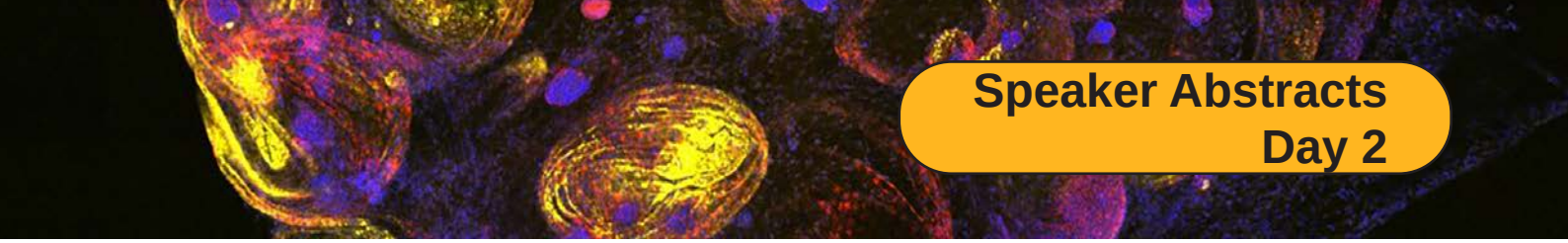
Division of Clinical Application Research, Center for iPS Cell and Application (CiRA), Kyoto University

ABSTRACT

We are currently advancing the development of artificial platelets derived from iPS cell–based immortalized megakaryocyte cell lines that lack HLA class I expression. These cell lines serve as master cell banks for platelet production in accordance with Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (GCTP) standards. A clinical study (iPLAT1) has already been conducted using autologous iPSC-derived artificial platelets for a patient with thrombocytopenia complicated by platelet transfusion refractoriness, confirming both the safety of the manufacturing process and the final product. In parallel, reverse translational research based on the findings of this clinical study has yielded several important insights. In this presentation, I will highlight some of these key findings through specific examples. Building upon these research outcomes, we are now collaborating with multiple industrial partners to drive the clinical development of next-generation artificial platelets, incorporating automated culture systems and continuous manufacturing processes.

BIO

Koji Eto was originally a clinical physician of cardiovascular medicine (M.D.). After clinical carriers in Tokyo, he joined The Scripps Research Institute, La Jolla, California. There he developed in vitro methods to differentiate mouse embryonic stem cells (ES cells) into megakaryocytes and platelets. He then moved to the Institute of Medical Science, The University of Tokyo, in 2003 (as assistant and associate professor). In 2011, he moved to CiRA as full professor (current position) and was also promoted as cross-appointed professor at Chiba University School of Medicine (2016~2024). He has realized the world's first clinical trial of human iPS cell-derived platelet products for a patient suffering from platelet transfusion refractoriness by alloimmunization. Now he is the Section leader of Clinical Application Research and Deputy Director of CiRA, Kyoto University.



Metabolic programming of muscle stem cells and muscle organoids

Shyh-Chang Ng

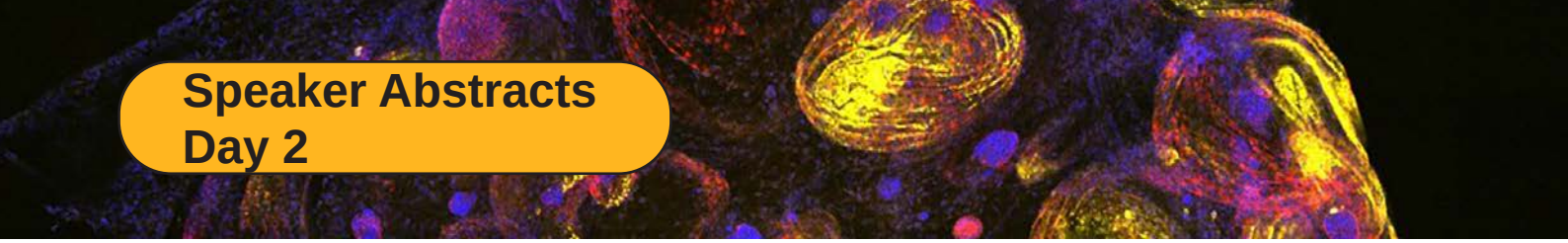
State Key Laboratory of Organ Regeneration and Reconstruction, Institute of Zoology, Chinese Academy of Sciences; University of Chinese Academy of Sciences; Beijing Institute for Stem Cell and Regenerative Medicine

ABSTRACT

Human GWAS have shown that obesogenic FTO polymorphisms correlate with lean mass, but the mechanisms have remained unclear. It is counterintuitive because lean mass is inversely correlated with obesity and metabolic diseases. Here, we use CRISPR to knock-in FTOrs9939609-A into hESC-derived tissue models, to elucidate potentially hidden roles of FTO during development. We find that among human tissues, FTOrs9939609-A most robustly affect human muscle progenitors' proliferation, differentiation, senescence, thereby accelerating muscle developmental and metabolic aging. An edited FTOrs9939609-A allele over-stimulates insulin/IGF signaling via increased muscle-specific enhancer H3K27ac, FTO expression and m6A demethylation of H19 lncRNA and IGF2 mRNA, with excessive insulin/IGF signaling leading to insulin resistance upon replicative aging or exposure to high fat diet. This FTO-m6A-H19/IGF2 circuit may explain paradoxical GWAS findings linking FTOrs9939609-A to both leanness and obesity. Our results provide a proof-of-principle that CRISPR-hESC-tissue platforms can be harnessed to resolve puzzles in human metabolism.

BIO

Shyh-Chang Ng is the PI of the Regenerative Metabolism Lab at the CAS Institute of Zoology and a full Professor at the University of Chinese Academy of Sciences. His lab is focused on investigating the nutritional and metabolic programming required for stem cell proliferation, differentiation and regeneration. He has won the HHMI International Scholar award, VcanBio Award for Innovations and Breakthroughs in Medicine, CAS Innovative Scientist of the Year award, CSSCR Stem Cell Investigator award, etc. He is the Chief Scientist of a NKRD Program grant, a member of the editorial boards for Cell Proliferation, JCSM, and the Chinese Gerontology and Geriatrics Society scientific advisory board. He has published over 60 papers in journals such as Science, Cell, Nature Medicine, Cell Stem Cell, Cell Metabolism, and Cell Research, with >12000 citations. He graduated with an A.B. (summa cum laude) from Princeton University, and a Ph.D. from Harvard Medical School.



Speaker Abstracts Day 2

Abstract selected talk

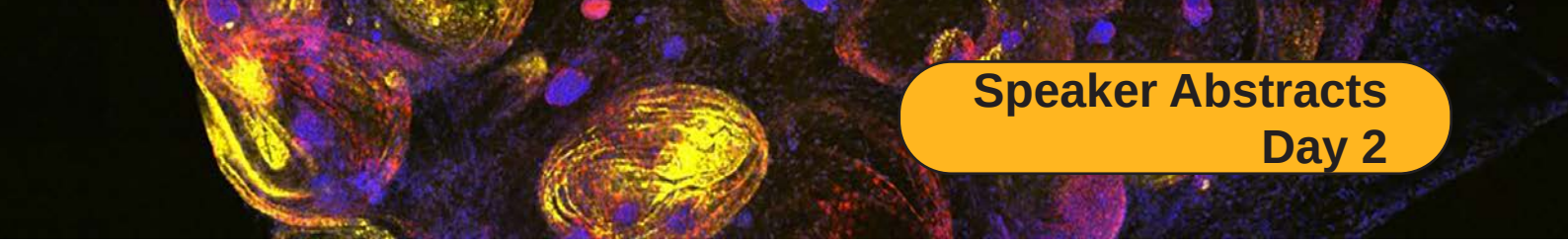
Making platelets from human adipose tissue-derived mesenchymal cells and the effect on a GVHD model using NOG mice

Ryo Tanaka[1,2], Atsuko Oyama[1,2], Miya Onodera[1,2], Shigeki Hijikata[2], Yumiko Matsubara[1,3]

[1]Center for Integrated Medical research, Keio University, Japan; [2]AdipoSeeds, Inc., Japan; [3]Institute for Sports Medicine, Keio University, Japan

ABSTRACT

We developed platelet-like cells from subcutaneous adipose tissues (PLC) (2019 Blood) for clinical applications. The PLC are a beneficial characteristic that the PLC can be stored for at least 1 year. Here we report the effect of PLC on a GVHD model using NOG mice. The 20 NOG mice irradiated at 1.5Gy was transplanted with 2.5-3 x 10^6 human peripheral blood mononuclear cells (PBMCs) into all mice through the tail vein to create a xeno-GVHD model. After PBMC transplantation, PLC 1×10^7 cells were administered to 10 mice via the tail vein (PLC group), and the remaining 10 mice were given vehicle (Vehicle group). Both the Vehicle and PLC groups showed weight loss after 1 week and developed GVHD, and the weight loss in the PLC group was slower than in the Vehicle group from 2 weeks. The decline in survival rate in PLC group was significantly slower than that in the Vehicle group (p=0.0135). The PLC group showed the reduction of lymphocyte infiltration and suppression of fibrosis. After PBMC transfer, alleviation of weight loss and a significant decrease in mortality rate were observed in the PLC group, suggesting that PLC has a GVHD suppressive effect.



Abstract selected talk

VHL deficient human kidney organoid to model clear cell renal cell carcinoma

Yixuan Wang, Huamin Wang, Ximing Gong, Meng Liu, Chao Zhang, Tian Zhang, Angelysia Cardilla, Mihir Yogesh Naik, Yun Xia

LKCMedicine, Nanyang Technological University, Singapore

ABSTRACT

The inactivation of Von Hippel-Lindau (VHL) tumor suppressor gene, found in approximately 90% of cases, was identified as the primary driver event of clear cell renal cell carcinoma (ccRCC) development. Existing genetic engineered mouse models have failed to fully capture the distinctive features of ccRCC, and understanding VHL mutation in comparable human cells has been limited. Newly developed 3D human kidney organoid comprises of segmentally patterned nephron structures, interstitium and vascular network, serving as a novel research model with higher physiological relevance. In this study, we developed a VHL knockout human kidney organoid model based on CRISPR/Cas9-engineered human embryonic stem cells. The absence of VHL triggered 'clear cell-like' phenotype in kidney tubular epithelium, a defining trait of ccRCC in clinics, and recapitulated key metabolism reprogramming observed in patients, including significant lipid and glucose metabolic alterations. Long-term culture of VHL deficient kidney organoids demonstrated increasing proliferation potential. This model offers an innovative platform for ccRCC research and treatment development.s

Stem cells and marrow ageing across the skeleton: The skull as a vulnerable niche

Anjali Kusumbe

Nanyang Technological University, Singapore

ABSTRACT

Bone marrow health is essential for blood formation, transplantation, and cancer outcomes, yet the bone marrow niche deteriorates with age. Our multi-laboratory investigation reveals that the skull marrow is among the most vulnerable sites of age-related decline. Integrative transcriptomic, proteomic, and imaging analyses show extensive loss of mesenchymal and osteoprogenitors, reduced angiogenic and lymphatic activity, vascular senescence, adipocyte accumulation, mitochondrial dysfunction, DNA replication stress, and chronic inflammation in ageing skull niches. In contrast, vertebral marrow remains relatively preserved. These findings redefine marrow ageing and identify the skull as a fragile, clinically important niche critical for sustaining blood and immune health. Ongoing work investigates how haematopoietic stem and progenitor cells (HSPCs) and mesenchymal stromal cells (MSCs) differ across skeletal sites to uncover the molecular and functional diversity shaping marrow health and ageing.

BIO

Anjali Kusumbe is an Associate Professor and Group Leader at Nanyang Technological University, Singapore, and a European Research Council Investigator and Group Leader at the Multidisciplinary Institute of Ageing in Portugal. She is recognized for her work on vascular–stem cell interactions and their role in tissue homeostasis, ageing, and regeneration. Her research focuses on uncovering how vascular niches orchestrate stem cell behavior and how age-associated vascular changes contribute to stem cell dysfunction, tissue degeneration, and impaired repair. Her lab integrates high-resolution imaging, single-cell and spatial omics, and genetic models to dissect the mechanisms by which blood vessels regulate stem cell function. Her contributions have been recognized through numerous prestigious awards, including the Werner-Risau Memorial Award from the German Society for Cell Biology, the Iain T. Boyle Memorial Award from the European Calcified Tissue Society, Women in Cell Biology Early Career Medal from the British Society for Cell Biology, the Life Sciences Award from the Royal Microscopical Society, Career Development Award from the Medical Research Council UK, Rising Star Award from the International Society for Regeneration Biology. She is also actively involved in international scientific communities and initiatives promoting early-career researchers and equity in science.

SCSS-Dr Susan Lim Award for Outstanding Young Investigator Presentation

Biomaterials to engineer human immune cells and tissues

Andy Tay[1,2]

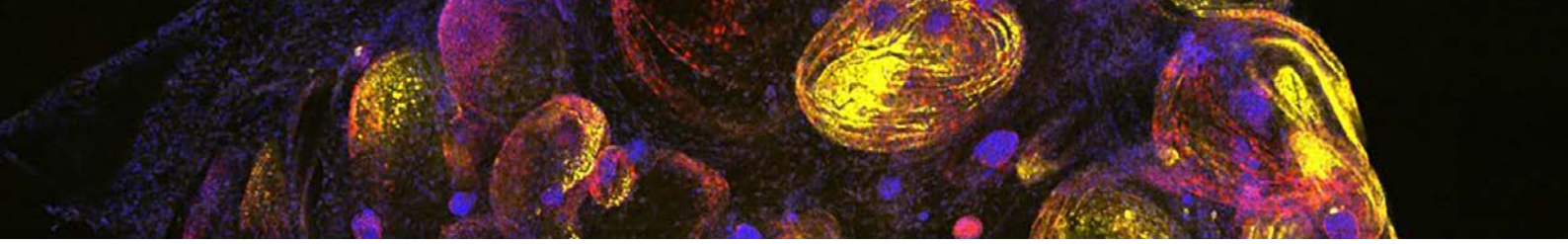
[1]Department of Biomedical Engineering, National University of Singapore, Singapore; [2]Institute for Health Innovation & Technology, National University of Singapore, Singapore

ABSTRACT

While significant advances have been made in the field of human immunology, we still lack tools and models to study immune cells within human tissues, and to engineer these primary immune cells. This is crucial because immune cells are known to exhibit variable phenotypes and functions in different tissue microenvironments. Immuno-engineering is an interdisciplinary field using approaches in immunology, bioengineering and material sciences to manipulate immunity for diagnostic and therapeutic purposes. Here, I will describe three tools and models my lab has developed to enable the study of human tissue immunology. I will first discuss an in vitro human immune organoid model that preserves high cell diversity, retains donor memory and can be educated to recognise naïve antigens. I will next describe a porous microneedle to extract tissue immune cells before ending with a nanotechnology for genetic engineering and nanobiopsy of diverse primary human immune cells.

BIO

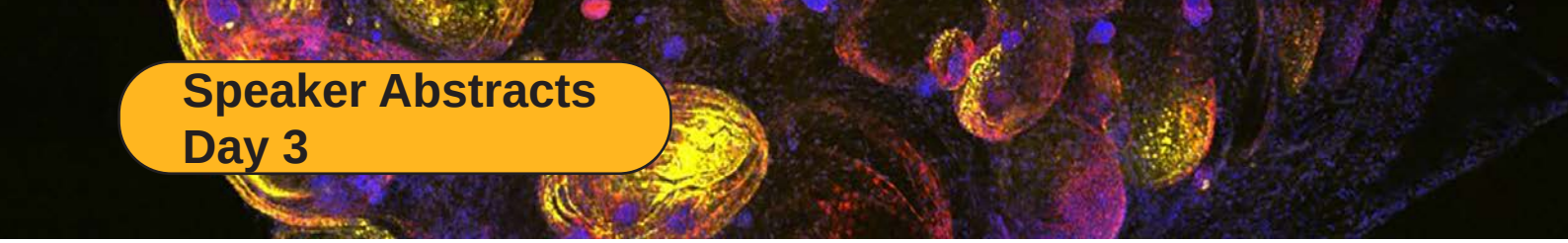
Andy Tay graduated in 2014 from NUS with a First-Class Honors in Biomedical Engineering. He later headed to the University of California, Los Angeles for his PhD studies and graduated in 2017 as the recipient of the Harry M Showman Commencement Award. Andy next received his postdoctoral training at Stanford University before heading to Imperial College London as an 1851 Royal Commission Brunel Research Fellow. He is currently a Presidential Young Professor in NUS. Andy is listed as a Forbes 30 Under 30 (US/Canada, Science), World Economic Forum Young Scientist and Top 2% Scientist in the World by Stanford University. He recently won the President's Science and Technology Award Young Scientist Award, the highest national accolade for researchers under 40 in Singapore.



SPEAKER ABSTRACTS

Day 3

14 Nov 2025



Speaker Abstracts Day 3

A decade of human midbrain-like organoids: Advances, discoveries, and future directions in Parkinson's Disease modeling and therapy

Hyunsoo Shawn Je

Neuroscience and Behavioral Disorders Programme, Duke-NUS Medical School, Singapore

ABSTRACT

Over the past decade, human midbrain-like organoids (hMLOs) have emerged as transformative tools for modelling Parkinson's disease (PD), a neurodegenerative disorder that affects millions of people worldwide. Although traditional rodent models have provided valuable insights, they cannot fully replicate the complex pathophysiology of human PD. This limits our progress in understanding the disease and developing effective therapies. In contrast, hMLOs, which are derived from human pluripotent stem cells, better mimic the key structural and functional features of the human midbrain, including the independent production of neuromelanin, which is a hallmark of PD. In this talk, I will trace the evolution of hMLO research, from early in vitro approaches to the latest technological advances. I will demonstrate how hMLOs have deepened our understanding of PD mechanisms, facilitated high-throughput drug screening and paved the way for cell replacement therapy, bringing us closer to breakthroughs in PD treatment.

BIO

Shawn Je is a tenured associate professor in the Neuroscience and Behavioural Disorders Programme at Duke-NUS Medical School in Singapore. He is also the director of the SingHealth Advanced Imaging Centre. He earned his Bachelor's degree from KAIST and his Master's from the University of Michigan. He completed his PhD through the NIH Graduate Partnership Programme, conducting research under Dr Bai Lu. Dr Je then completed a postdoctoral fellowship at the Howard Hughes Medical Institute/Duke University Medical School under the supervision of Dr Michael Ehlers. He joined Duke-NUS as an Assistant Professor in late 2010, being awarded tenure in 2017. In 2022, he received the Scientist of the Year Award from South Korea's Ministry of Science and ICT. Dr Je's research, supported by government agencies and private foundations in Singapore and Australia, focuses on advancing neuroscience through innovative imaging and translational approaches.

Novel roles of the epigenetic repressor SMCHD1 in regulating spermatogonial stem cell maintenance

Shifeng Xue

Department of Biological Sciences, National University of Singapore, Singapore

ABSTRACT

Spermatogonial stem cells (SSCs) are adult stem cells that ensure continuous spermatogenesis throughout life. While modeling Bosma Arhinia Microphthalmia Syndrome mutations, we knocked in the most common patient mutation in SMCHD1 (p.His348Arg; SMCHD1H348R) into mice. Unexpectedly, we uncovered a novel role for the epigenetic repressor SMCHD1 in regulating SSC maintenance. SMCHD1H348R/H348R male mice were infertile, while females and heterozygotes were unaffected. This mutation caused loss of the protein's canonical repressive function, which was independent of its effect on spermatogenesis. Profiling of germ cells revealed epigenetic dysregulation of genes involved in maintenance of stemness, including upregulation of ID proteins and downregulation of PLZF. We suggest that the H348R mutation change interaction dynamics of SMCHD1 with binding partners involved in the regulation of genes important for SSC maintenance. Together, our findings reveal novel roles of SMCHD1 in regulating SSC maintenance, which may also help us understand regulatory mechanisms in other adult stem cells.

BIO

Shifeng Xue obtained her PhD in developmental biology from University of California, San Francisco. She did a postdoctoral training at A*STAR, Singapore in human genetics. She is currently an assistant professor at the National University of Singapore. She was awarded the Young Scientist Award by the Singapore National Academy of Sciences in 2018 and the L'oreal-UNESCO For Women In Science Singapore Award in 2023. Her lab studies epigenetic regulation in development and disease, with a particular focus in epigenetic regulators involved in rare genetic diseases.

Speaker Abstracts Day 3

Refining human brain organoid models to capture human-specific features

Hongyan Wang

Neuroscience & Behaviroal Disorders Programme, Duke-NUS Medical School, Singapore

ABSTRACT

Human cerebral organoids provide a powerful platform to model early brain development and uncover mechanisms underlying neurodevelopmental disorders. By recapitulating key cellular and molecular events of corticogenesis, organoids offer opportunities to dissect human-specific features of brain development and their perturbation in disease states. we have identified a signaling pathway that promotes human cortical expansion by regulating the production of outer radial glial cells, a primate-enriched neural stem cell population critical for cortical growth. Out studies illustrate how organoid-based approaches can uncover disease-associated mechanisms and human-specific neurodevelopmental programs, underscoring their utility as a versatile system for modeling neurodevelopmental disorders.

BIO

Hongyan Wang is Professor and Acting Director of the Neuroscience & Behavioral Disorders Program at Duke-NUS Medical School, Singapore. Her laboratory uses Drosophila as a model to study the reactivation of quiescent neural stem cells. Her lab also investigates cortical development in mice, human brain development using brain organoids, and the underlying causes of neurodevelopmental disorders. She is an elected EMBO Associate Member, the founding president of Society of Developmental Biologists Singapore, Vice-President of Stem Cell Society Singapore, and co-chair of Singapore Rare Disease Models and Mechanisms Network.

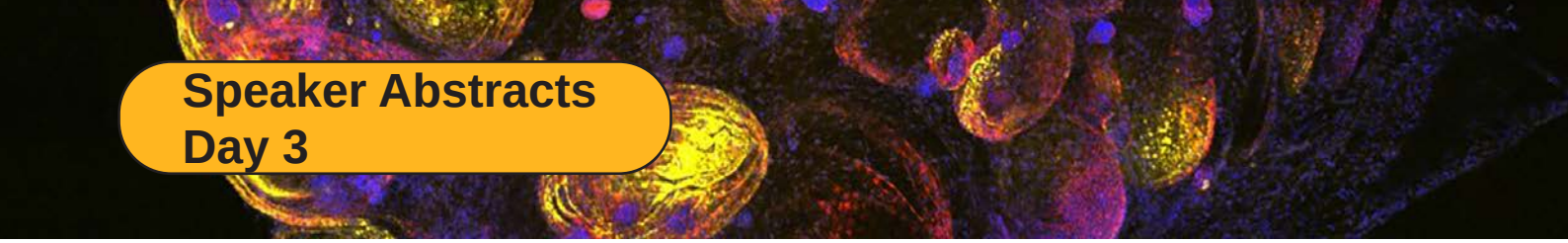
Epithelial WNT secretion drives niche escape of developing gastric cancer

Jaehun Lee[1,2], Soomin Kim[1,3], Youngchul Oh[1,2], Jihoon Kim[1,4], Stephan R. Jahn[5], Isaree Teriyapirom[6,7], Yeongjun Kim[1,3], Sang-Min Kim[8], Tim Schmäche[5,9], Jungmin Kim[10,11,12], Somi Kim[2], Anne-Marlen Ada[5], Andrea Català-Bordes[1], Youngwon Cho[13,14], Jinho Kim[17,18,19], Amanda Andersson-Rolf[6], Sebastian R. Merker[5], Joo Yeon Lim[10], Ji-Yeon Park[20], Thomas M. Klompstra[1,21], Ki-Jun Yoon[21,22,23], Ho-Seok Lee[1,3], Jong Kyoung Kim[2], Eunyoung Choi[13,14,15], James R. Goldenring[13,14,15,16], Jae-Ho Cheong[10,11,12,24,25,26], Hyunki Kim[8], Daniel E. Stange[5,9,27], Heetak Lee[1], Bon-Kyoung Koo[1,2,22], and Ji-Hyun Lee[1,28]

[1]Center for Genome Engineering, Institute for Basic Sciences, Republic of Korea; [2]Department of Life Sciences, Pohang University of Science and Technology (POSTECH), Republic of Korea; [3]Department of Biology, Kyung Hee University, Republic of Korea; [4]Department of Medical and Biological Sciences, The Catholic University of Korea, Republic of Korea; [5]Department of Visceral, Thoracic and Vascular Surgery, Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany; [6]Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna BioCenter (VBC), Austria; [7]Vienna BioCenter PhD Program, Doctoral School of the University of Vienna and Medical University of Vienna, Austria; [8]Department of Pathology, Yonsei University College of Medicine, Republic of Korea; [9]National Center for Tumor Diseases (NCT), NCT/UCC Dresden, a partnership between DKFZ, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, and Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Germany; [10]Department of Surgery, Yonsei University College of Medicine, Republic of Korea; [11]Severance Biomedical Science Institute, Yonsei University College of Medicine, South Korea; [12]Department of Medical Science, Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Republic of Korea; [13]Section of Surgical Sciences, Vanderbilt University Medical Center, Tennessee, USA; [14]Epithelial Biology Center, Vanderbilt University Medical Center, Tennessee, USA; [15]Department of Cell and Developmental Biology, Vanderbilt University, Tennessee, USA; [16]Nashville VA Medical Center, Tennessee, USA; [17]Precision Medicine Center, Future Innovation Research Division, Seoul National University Bundang Hospital (SNUBH), Republic of Korea; [18]Department of Genomic Medicine, Seoul National University Bundang Hospital, Seongnam, Gyeonggi-do 13620, Republic of Korea; [19]Department of Laboratory Medicine, Seoul National University Bundang Hospital, Republic of Korea; [20]Gradiant Bioconvergence Inc., Republic of Korea; [21]Department of Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST), Republic of Korea; [22]Graduate School of Stem Cell and Regenerative Biology, KAIST, Republic of Korea; [23]KAIST Stem Cell Center, KAIST, Republic of Korea; [24]Department of Biochemistry and Molecular Biology, Yonsei University College of Medicine, Republic of Korea; [25]Chronic Intractable Disease for Systems Medicine Research Center, Yonsei University College of Medicine, Republic of Korea; [26]Department of Biomedical Systems Informatics, Yonsei University College of Medicine, Republic of Korea; [27]Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany; Helmholtz-Zentrum Dresden-Rossendorf (HZDR), German; [28]Department of Biological Sciences, Sungkyunkwan University,, Republic of Korea

ABSTRACT

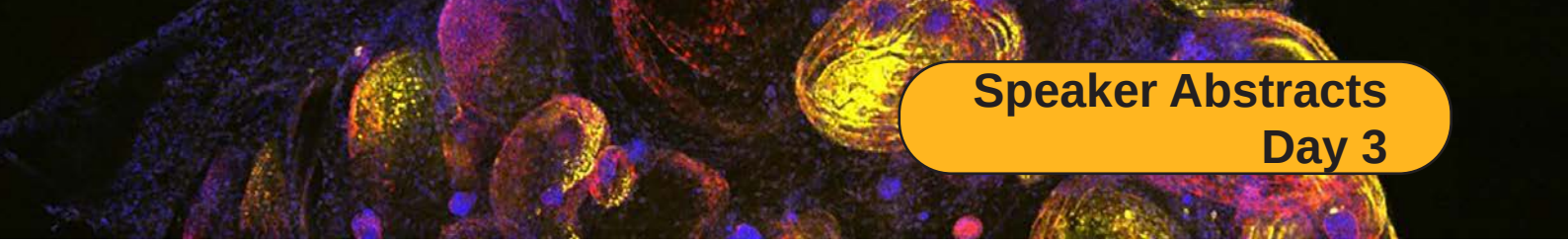
WNT signaling is essential in cancer development, with APC mutations driving colon cancer. In gastric cancer, however, APC and CTNNB1 mutations are rare, and the mechanisms of WNT self-sufficiency remain unclear. Using gastric organoids and mouse models, we found that mesenchymal WNTs maintain the normal epithelium, while KRAS activation induces epithelial WNT secretion, enabling WNT self-sufficiency. Single-nucleus multiomics revealed that KRAS–MAPK signaling activates SMAD2/3, opening the WNT7B locus and generating WNT7B+



epithelial niche cells. In human gastric cancer, epithelial WNT production arises via HER2-mediated KRAS–MAPK activation or WNT2 amplification. Analysis of cancer cell line data further indicates that the KRAS–MAPK–WNT7B axis operates in other cancers, including lung cancer. These findings identify epithelial WNT secretion as a central mechanism of WNT self-sufficiency in gastric tumorigenesis. Unlike APC/CTNNB1 mutations in colon cancer, this process is targetable, offering potential therapeutic opportunities.

BIO

Ji-Hyun Lee, Ph.D., is a Research Fellow (Junior Principal Investigator) at the Center for Genome Engineering, Institute for Basic Science (IBS), Daejeon, and an Adjunct Professor in the Department of Biological Sciences at Sungkyunkwan University, Korea. She earned her B.S. and completed a combined M.S./Ph.D. in Systems Biology at Yonsei University in 2015, where she investigated the molecular and cellular mechanisms of wound healing in Drosophila. As a postdoctoral fellow at IMBA (Vienna) in Dr. Bon-Kyoung Koo's laboratory, she shifted her focus to mouse genetics and organoid systems to study adult stem cell biology in regeneration. Since joining IBS in 2022, she has led a research team exploring adult stem cell biology, gastric cancer initiation, and the stomach–brain axis using organoid technology, next-generation sequencing, and mouse models. Dr. Lee has co-authored multiple high-impact publications, including in Cell Stem Cell, Nature Communications, Science Advances, and Genome Research.



Abstract selected talk

Investigating thymic involution through thymic organoids

Jia Ming Nickolas Teo, Yuin-Han Loh

*Institute of Molecular and Cell Biology (IMCB), A*STAR (Agency for Science, Technology and Research), Singapore*

ABSTRACT

As a crucial site of T cell education, the thymus is important for preventing autoimmunity, and nurturing thymocytes effective against threats such as pathogens and cancer. Despite this important role, thymic involution can begin as soon as 1 year of age, with the progressive loss of thymic organization leading to numerous impairments in immune function. Furthermore, during open heart surgery, standard operating procedure typically involves partial or total thymectomy, with detrimental consequences such as reduced peripheral lymphocytes and increased all-cause mortality. Therefore, investigations into slowing thymic degeneration and promoting thymus regeneration are important for maintaining immune health for all. To model thymic involution and discover approaches for sustaining thymic functions, thymus organoids were differentiated from hESCs. Adapting an established differentiation protocol, hESCs are assembled into embryoid bodies before undergoing differentiation whilst exposed to a liquid-air interface on transwells. Several drugs were screened for their ability to further promote thymus organoid development. hESC-derived HPSCs were also introduced after organoid establishment to validate organoid functionality and assess changes in T cell education. Consequently, a functional organoid model was established, with further work ongoing to increase organoid complexity and relevance through introducing additional cell types.

Organoids Zoo - a new platform for animal science

Bon-Kyoung Koo

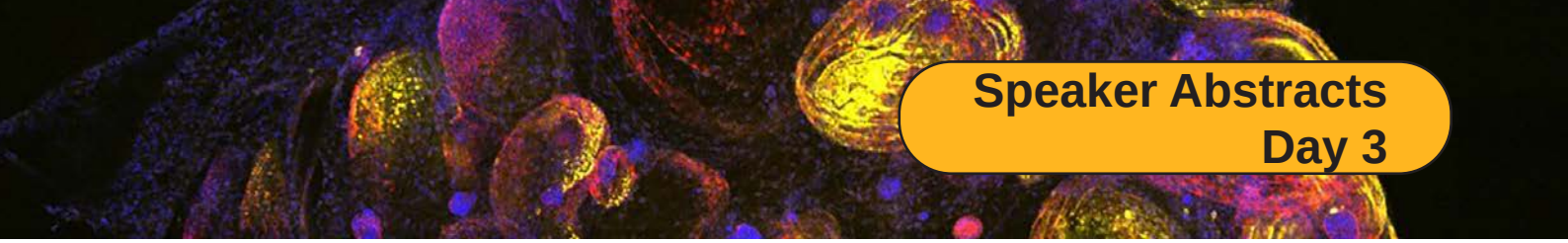
Center for Genome Engineering, Institute for Basic Science, Daejeon, S. Korea

ABSTRACT

Here, we established a cross-species “organoid zoo” of adult stem cell–derived intestinal organoids from 26 vertebrate species, spanning rodents, bats, avians, pets, farm animals, and experimental models, including mice, rats, ferrets, minipigs, and primates. These diverse organoids can be robustly maintained in a unified, commercially available medium, enabling systematic cross-species analysis at scale. We demonstrate the platform’s versatility through applications including single-cell RNA sequencing, biobanking, regeneration assays, genome editing, viral infection modeling, and drug screening. Comparative transcriptomics identified Solute Carrier Family 12 member 2 (Slc12a2) and Cyclin-Dependent Kinase 6 (Cdk6) as conserved intestinal stem cell markers. Functionally, spiny mouse organoids showed enhanced regeneration via a YAP-enhanced stem cell population, and livestock organoids modeled species-specific viral susceptibility. Importantly, we demonstrate that genetic manipulation is feasible in non-experimental animal models. The organoid zoo provides a scalable and versatile framework to systematically investigate regeneration, disease, and fundamental biology across the animal kingdom.

BIO

Bon-Kyoung Koo is a mammalian geneticist studying E3 ubiquitin ligases—including Mib1 (Dev 2005, Neuron 2008), Rnf43 (Nature 2012, PNAS 2015), and Phf16 (Dev Cell 2024)—that regulate Notch, Wnt, and Hippo signaling in development, regeneration, and tumorigenesis. He revealed how signaling pathways are controlled by ubiquitin-mediated endocytosis and proteolysis, identifying Rnf43 and Znrf3 as tumor-suppressive membrane E3 ligases that degrade Wnt receptors via endo-lysosomal trafficking. He also defined key phosphorylation sites (Nat Commun 2020) and downstream mediators Daam1/2 (Sci Adv 2023), enabling their use in proteolysis-targeting antibodies (PROTABs). Dr. Koo pioneered genetic technologies—viral and BAC transgenesis, CRISPR/Cas9, and conditional knockouts—to establish adult stem cell-derived organoid systems (Nat Rev MCB 2020). His lineage-tracing studies defined Troy+ and isthmus gastric stem cells (Cell 2013; CSC 2019) and stem cell quiescence (CSC 2022). Recently, he developed mosaic genetics tools (Nature 2021; Nat Commun 2024) enabling fly-like genetic precision in mice.



KEYNOTE LECTURE

Age-Related Macular Degeneration: What goes wrong, how to fix it

Nurten Akturk, Affan Sheik, Emily A. Swanzey, Tracy McGarr and Martin F. Pera

JAX Mammalian Genetics, the Jackson Laboratory, Bar Harbor ME USA

ABSTRACT

Age-related macular degeneration (AMD) is the most common cause of blindness in our aging population. Using human induced pluripotent stem cells (iPSC), we have modelled the effects of the TIMP3 p. (Ser38Cys) mutation on retinal pigment epithelium (RPE), a key target cell in this disease. We observed altered deposition of extracellular matrix and loss of structures resembling basal infoldings, changes which could compromise transport and barrier functions of the RPE. We are also developing a second-generation iPSC therapy for AMD aimed at replacing both RPE and lost photoreceptors. Our approach is based on the known capacity of the RPE to regenerate the neural retina in lower vertebrates, and employs cellular grafts composed of iPSC derived wild-type RPE combined with RPE that has been engineered to undergo reprogramming into the photoreceptor lineage. Reprogramming through overexpression of the transcription factor NGN2 leads to rapid and facile conversion of RPE into progenitors that differentiate further to photoreceptor-like cells.

BIO

Martin Pera is a Professor at the Jackson Laboratory. Pera's research focus is the cell biology of human pluripotent stem cells. His laboratory at Monash University was the second in the world to isolate embryonic stem cells from the human blastocyst, and the first to describe their differentiation into somatic cells in vitro. Pera was amongst the first to analyze heterogeneity in human pluripotent stem cell cultures, work that has clarified the embryological coordinates of these cells and is critical to their use as models for human development. His research on neural differentiation of human pluripotent stem cells helped lead to the development of a new treatment for macular degeneration, a common form of blindness, now in clinical trial in Israel and California. At the Jackson Laboratory, he is using human stem cells to study the genetics of age-related macular degeneration and to develop new approaches to cell therapy of the disease.

Modelling cardiovascular-metabolic biology with iPS cells

Roger Foo

Cardiovascular Metabolic Translational Research Programme, NUHS, Singapore; Cardiovascular Research Institute, NUS Yong Loo Lin School of Medicine, Singapore

ABSTRACT

The Foo lab makes use of the ES cell, iPS cell and animal cell models for the purpose of gene candidate discoveries. Gene expression regulation underpins cardiac cell state transitions, and the recognition of gene control switches points to potential new therapeutic or disease biomarker options. Here, we have used the genome-wide CRISPR approach and uncovered a molecular candidate, which mediates a mechanism as part of the cell adherens junction complex, that is necessary for cardiomyocyte differentiation. Conversely, a separate genome-wide screen identifies a marker gene for cardiomyocyte dedifferentiation which we find a gateway to precede cardiomyocyte regeneration. Both projects raise the interesting question of whether cardiomyocytes journey back up the hill of the epigenetic landscape (dedifferentiation) is simply the reverse of its journey downhill (differentiation).

BIO

Roger Foo is Zayed bin Sultan Al Nahyan Professor at the NUS School of Medicine, Vice Dean of Research, Director NUHS Cardiovascular Metabolic Disease Translational Research Programme, Cardiovascular Research Institute, Advisor to the NUHS Clinician Scientist Academy, and Senior Consultant Cardiologist, National University Heart Centre. He is an NUS med school graduate, and spent 20 years abroad on specialist training before returning to Singapore in 2013. His training was undertaken at Kings College Hospital, London, and Addenbrooke's Hospital, Cambridge. He was Wellcome Trust Fellow at Albert Einstein College of Medicine, New York, and returned to Cambridge to start a group as British Heart Foundation Fellow and Consultant Physician, before eventually returning to Singapore. His lab was the first to publish an epigenomic map of the failing human heart. More recently, he has published an in-depth analysis of the human cardiac chromatin 3D organisation, elucidating its changes during the heart disease response. The lab deep dives into the heart epigenome in continuing aspirations to discover mechanisms of disease for new therapies or biomarkers. Today, he spends a lot of time mentoring young scientist, alongside growing research on heart disease prevention and targets for new drug development.

Matrix matters: Laminin-guided differentiation of cardiovascular progenitors from pluripotent stem cells

Swarnaseetha Adusumalli[1], Christabel Chan[1], Wei Qian Heng[2], Xin Yi Cheng[1], Lynn Yap[1,3]

[1]Lee Kong Chian School of Medicine, NTU, Singapore, [2]Temasek Polytechnic, Singapore,3National Heart Center, Singapore

ABSTRACT

Ischemic heart disease continues to pose a major global health burden, despite advances in medicine. In this talk, I will present a chemically defined and reproducible method to generate cardiovascular progenitor cells (CVPs) from pluripotent stem cells using specific laminin substrates. While LN521 supports pluripotency and stem cell proliferation, we used LN221, expressed in cardiac tissue, as a differentiation matrix to promote mesodermal lineage commitment. Phenotypical morphology observation revealed that although both LN521 and LN221 generate CVPs that mature into beating cardiomyocytes, single cell RNA sequencing revealed several differences. LN221 significantly upregulates cardiac-related genes (e.g., TNNT2, MYL4, RYR2), while LN521 shows enrichment of mesodermal progenitor markers (ISL1, MEF2C, PDGFRA). Flow cytometry also confirmed higher cardiac marker expression in LN221-derived cells. Notably, early upregulation of Wnt pathway genes suggests a priming effect preceding CHIR99021 induction in LN221 matrix. Our findings highlight how matrix composition influences stem cell fate and differentiation efficiency, offering important insights for generating clinically relevant CVPs for cardiac regenerative therapies.

BIO

Lynn Yap is an interdisciplinary stem cell biologist with a Ph.D. from the NUS Graduate School for Integrative Sciences and Engineering. She completed her postdoctoral training at Duke-NUS Medical School, where she co-developed and out-licensed a laminin-derived cardiovascular progenitor technology aimed at treating ischemic cardiomyopathy. She is currently an Assistant Professor of Cardiometabolic Medicine at the Lee Kong Chian School of Medicine, with a joint appointment at the National Heart Research Institute Singapore. Her research focuses on uncovering the molecular and physiological mechanisms behind stem cell-based therapies for regenerative cardiology. She is a member of the International Society for Stem Cell Research, Stem Cell Society Singapore, American Heart Association, serves on the Early Career Advisory Group for eLife Sciences Publications, and a scientific co-founder of Alder Therapeutics.

Speaker Abstracts Day 3

Modelling acquired cardiac diseases with iPSCs: Insights from diabetic heart failure

Chrishan Ramachandra[1], Shuo Cong[2], Valerie Ho[1], Derek Hausenloy[2]

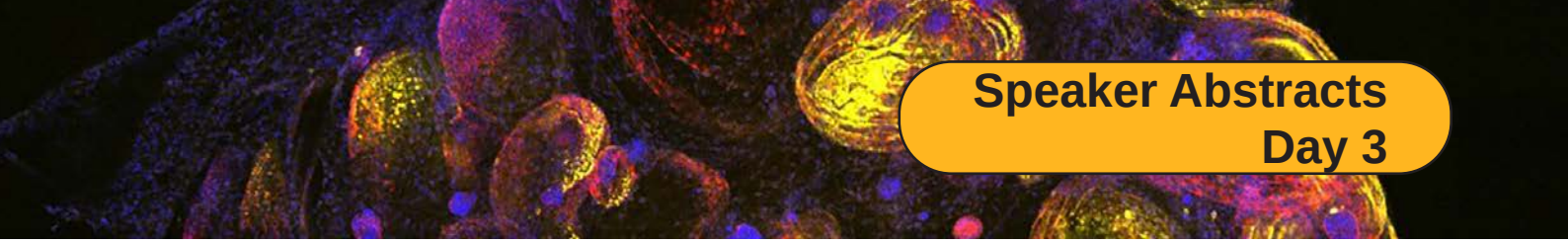
[1]National Heart Research Institute Singapore, National Heart Centre Singapore, Singapore; [2]Cardiovascular and Metabolic Disorders Program, Duke-NUS Medical School, Singapore

ABSTRACT

iPSCs have traditionally been used to model cardiac diseases driven by known genetic mutations, but whether iPSCs can also recapitulate acquired cardiac diseases with no clear genetic origins remains unclear. In this study, we modelled diabetic heart failure (DHF) using iPSCs derived from both healthy volunteers and DHF patients. Differentiated cardiomyocytes from DHF iPSCs exhibited structural, functional, and metabolic characteristics consistent with the patients' clinical profiles. Furthermore, we used these DHF cardiomyocytes to investigate whether the SGLT2 inhibitor empagliflozin exerts a direct effect on cardiomyocytes. Not only did empagliflozin improve the disease phenotype in these DHF cardiomyocytes, but we also identified a novel mechanism underlying its cardioprotective effects. In conclusion, our findings demonstrate that iPSCs can model acquired cardiac diseases, offering new insights into DHF pathophysiology and establishing a platform for drug screening, target discovery, and mechanistic studies.

BIO

Chrishan Ramachandra is a Principal Investigator at the National Heart Research Institute Singapore and Assistant Professor in the SingHealth Duke-NUS Cardiovascular Sciences Academic Clinical Programme. His work focuses on modelling cardiac diseases using induced pluripotent stem cells (iPSCs) to discover personalised therapeutics and new treatment targets for heart failure. He has made significant contributions to understanding cardiomyocyte differentiation, identifying key signalling networks, and advancing iPSC-derived cardiomyocyte maturation. His research on Long QT Syndrome type 2 uncovered novel molecular mechanisms and potential treatments, while his investigation into hypertrophic cardiomyopathy revealed myeloperoxidase as a therapeutic target. More recently, he has established patient-specific iPSC models of cardiometabolic disease for identifying and validating new therapeutic targets. His innovative work has earned him various awards and has yielded crucial insights into heart failure mechanisms, with some identified treatments currently undergoing clinical evaluation.



Abstract selected talk

Mapping Stress Response-QTLs using iPSC-cardiomyocytes for heart failure

Brandon Tan[1], Zi Hao Lin[1], Sze Woei Ng[1,2], Ecclesia Chong[1], Yuan He Ma[1], Sae Yeoh Ahpa[1], Wei Qiang Seow[1,2], Roger Foo[1,2]

*[1]Department of Medicine, National University Singapore, Singapore; [2]ATTRaCT Programme, Agency for Science Technology and Research (A*Star), Singapore*

ABSTRACT

Heart failure (HF) with preserved ejection fraction (HFpEF) is a growing global epidemic with limited therapeutic options. Human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) are a powerful resource to investigate how genetic variation shapes cardiomyocyte responses in stress and disease. We employ a 'cell-village' approach, pooling 120 participant iPSCs from the PICMAN study (ASCVD risk >5%), differentiating them into CMs and subjecting them to a metabolic-inflammatory cocktail. The perturbation mimics common HFpEF risk factors such as hyperglycaemia and hyperlipidaemia, inducing cellular metabolic and diastolic dysfunction - common features observed in HFpEF individuals. Through single-cell combinatorial indexing, and integrating donor whole-genome sequences, we demultiplex individual participants within the village and identify individual transcriptomic responses. Transcriptomic profiling of stressed versus control iPSC-CMs allows the identification of response expression quantitative trait loci (reQTLs) – genetic variants that modulate transcriptional responses to HFpEF-like stress. By colocalizing these reQTLs with GWAS signals for HF and other human heart tissue datasets, we aim to refine causal candidate genes and pathways contributing to HF pathophysiology. Overall, this work establishes a scalable, cost-effective framework for linking genetic variation to disease-relevant cellular mechanisms, with the potential to uncover new therapeutic targets for HFpEF.

Mitochondrial transplantation as a novel therapeutic strategy for cardiometabolic disorders

Qian Hua Phua[1,2], Jeremy Kah Sheng Pang[1], Hongjie Zhang[1,3,4], Winanto[1,2], Xiaoxiao Ma[1,5], Low Kay En[6], Shi Yan Ng[1,7], Boon Seng Soh[1,2]

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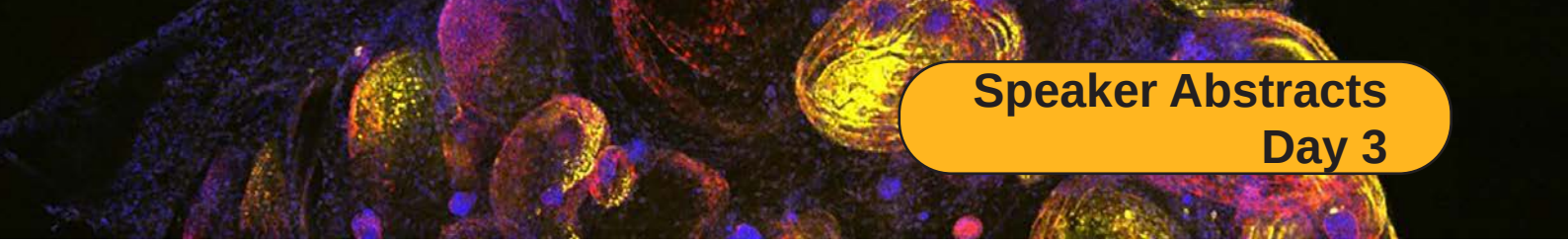
ABSTRACT

Mitochondrial dysfunction underlies a broad spectrum of inherited and age-related disorders. In mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS), mutations in the mitochondrial genome impair energy production and cellular function. We show that introducing healthy donor mitochondria into MELAS endothelial cells enhances metabolic activity and reduces mutant mitochondrial DNA load, leading to measurable functional recovery. These improvements are accompanied by increased protein translation and restored energy metabolism. Building on these findings, we applied mitochondrial therapy to a SIRT6 knockdown model of induced pluripotent stem cell (iPSC)-derived cardiomyocytes to simulate cardiac aging. The transfer of healthy mitochondria attenuated aging phenotypes, improved mitochondrial respiration, and strengthened contractile performance. Collectively, these results highlight the potential of mitochondrial therapy to rejuvenate cellular function and provide a promising approach to treating both genetic and age-related mitochondrial dysfunction.

BIO

Boon Seng Soh is a Principal Investigator at A*STAR's Institute of Molecular and Cell Biology. He earned his PhD from Imperial College London and completed postdoctoral training at Harvard University under Professor Kenneth Chien, where he studied multipotent cardiac stem cells and their microenvironment. Dr. Soh developed a 3D chambered cardiac organoid model and uses advanced analytical tools to study human heart development and disease. His research focuses on cardiac disease modeling, aging, and metabolism, with a particular interest in mitochondrial therapy (mitotherapy) to restore cellular function in mitochondrial disorders and age-related heart decline. Through his work, he seeks to bridge the gap between fundamental research and new therapies that can directly benefit patients with heart disease.



AASCRM LECTURE – Australasian Society for Stem Cell Research

Using iPSCs to model enteric nervous system development and for cell therapy

Lincon Stamp

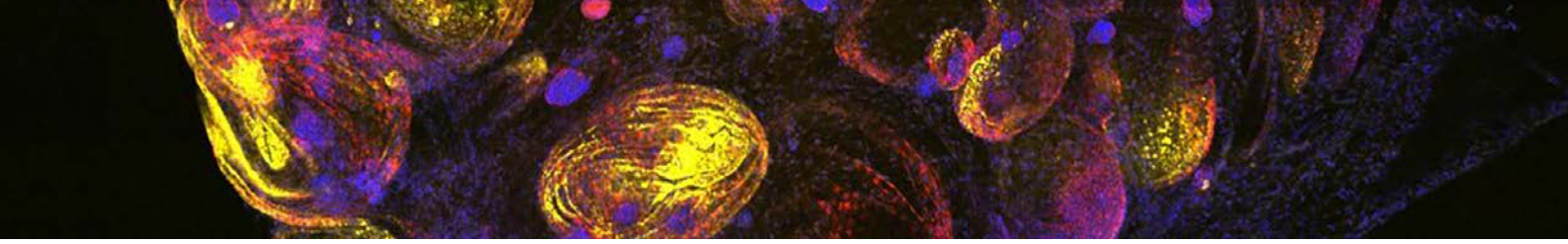
Department of Anatomy and Physiology, University of Melbourne, Australia

ABSTRACT

Understanding the development, function, and communication of the enteric nervous system (ENS) in humans is essential for developing new therapies for enteric neuropathies. In vitro modeling of this complex neural network using human induced pluripotent stem cells (hiPSCs) has enabled the study of enteric neuronal and glial development and function. Using functional calcium imaging, we characterised the maturation of hiPSC-derived enteric neurons and glia. Network analysis demonstrated critical roles for specific neurons in network communication and dispersed organisation of strongly connected modules. Furthermore, we aimed to assess the efficacy of stem cell therapy to regenerate the ENS in a novel rat model of Hirschsprung disease. Enteric neural precursors derived from hiPSCs were transplanted, with or without functionalised biomimetic hydrogels, into the distal colon of Ednrb-/- rats. Human enteric neural precursors survived and gave rise to mature neurons of various neurochemical phenotypes, with axon-like projections, providing a potential treatment for Hirschsprung disease.

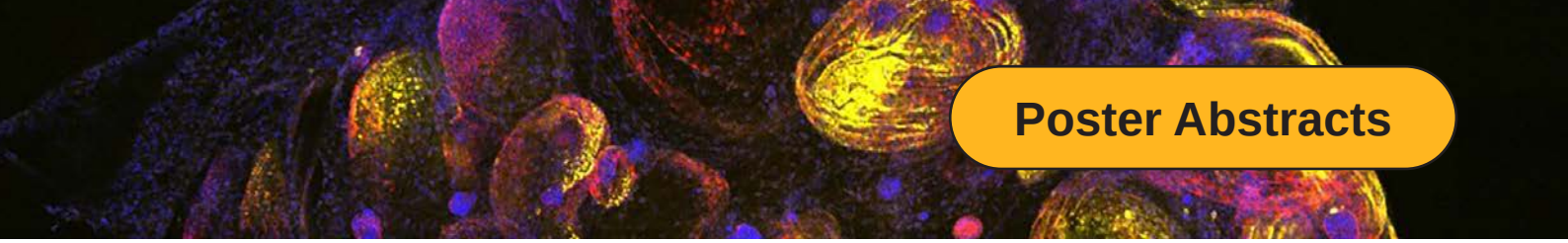
BIO

Lincon Stamp is a Group Leader in the Department of Anatomy and Physiology at the University of Melbourne, Australia and is the current President of the Australasian Society for Stem Cell Research (ASSCR). His lab, which he runs together with Dr Marlene Hao, is focused on the development, plasticity, and cell and gene therapies for the digestive system, with a particular focus on the enteric nervous system. Lincon and Marlene's work sits at the nexus of stem cell biology, enteric neuroscience and gastroenterology, with a primary aim of developing advanced stem cell therapies to treat currently intractable and debilitating gastrointestinal motility disorders. This work has led to publication of seminal studies in key journals including JCI, Gastroenterology and Stem Cell Reports.



POSTER

ABSTRACTS



Poster Abstracts

P1

Validating functional cardiomyocyte-specific histone-acetylated variants enhancers in human ES-derived Cardiomyocytes using a STARR-seq approach

Matias I Autio[1,2*], Chang Jie Mick Lee[2,3*], Chris Chow[5], Li Zhe[1], Chukwuemeka George Anene-Nzelu[4], Wilson Lek Wen Tan[1,2], Nathan Palpant[5], Roger S-Y Foo[2,3]

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Background: Genome-wide association studies have identified a large number of SNPs associated with cardiovascular disease, which tend to be located in the Cis-regulatory elements of the non-coding genome, such as enhancers, that can modulate the transcriptional activity of its target genes. However, the functional activity of these underlying SNPs in specific cardiac cell types can differ, and biological mechanisms of these genetic variations remain largely unexplored. Methods: Previously, we have mapped out 47,321 putative human cardiac enhancers and promoters from 70 left ventricular samples and have identified 1680 differential histone acetylome-wide association with its underlying putative SNP based on our histone acetylation quantitative trait locus (haQTL) analysis. To assess the enhancer activity of putative SNP in cardiomyocytes, we performed self-transcribing active regulatory region sequencing (STARR-seq. Here, we transfected a plasmid library containing 100,000 unique oligo-constructs bearing 16 unique 2bp barcodes, capturing 1680 unique haQTLs loci containing the reference and alternative SNP allele into H9 ES-derived cardiomyocytes. Hence, this allows for high-throughput validation of cardiomyocyte-specific variants with altered enhancer activity of varying effect sizes. Through GWAS co-localization and mapping cardiac cell-type epigenome data, we also explore the biological significance of enriched STARR-seq loci and their relevance in human population studies. Results: We have identified 1105/1680 significantly functional cardiac haQTL of varying effect sizes in human H9 hESC-derived cardiomyocytes. Additionally, 40/62 unique loci identified by colocalization of haQTLs with subthreshold loci of heart-related GWAS datasets were shown to have regulatory activity in cardiomyocytes. Interestingly, amongst the top STARR-seq hits, the variants rs5758468 and rs11663468 were also identified and validated previously to show disruption to MEF2A binding and the corresponding loss of H3K27ac peak height in cardiomyocytes. Using luciferase assay in derived-cardiomyocytes, we have also validated the concomitant reduction in luciferase activity, in the same direction as the STARR-seq assay, but not the non-significant SNPs. Additionally, through overlapping of H3K27ac enhancer HiChIP, and chromatin accessibility data, the majority of SNPs within cardiac enhancers validated by STARR-seq are connected to a distal gene by activity-by-contact (ABC) model. Concordant with Posterior inclusion probability (PIP) analysis, our results have also prioritized functional cardiomyocyte-specific SNPs, that were previously enriched in GWAS studies implicated in cardiomyocyte electrophysiology, such as Atrial Fibrillation. Conclusion: Taken together, our results have adopted an unbiased approach to prioritize functional cardiomyocyte regulatory elements, which help delineate target genes at cardiovascular GWAS loci implicated in cardiac disease and function. We anticipate combining single-cell multiome approaches would help expand the active enhancer repertoire regulating cardiac function in other given cell types.

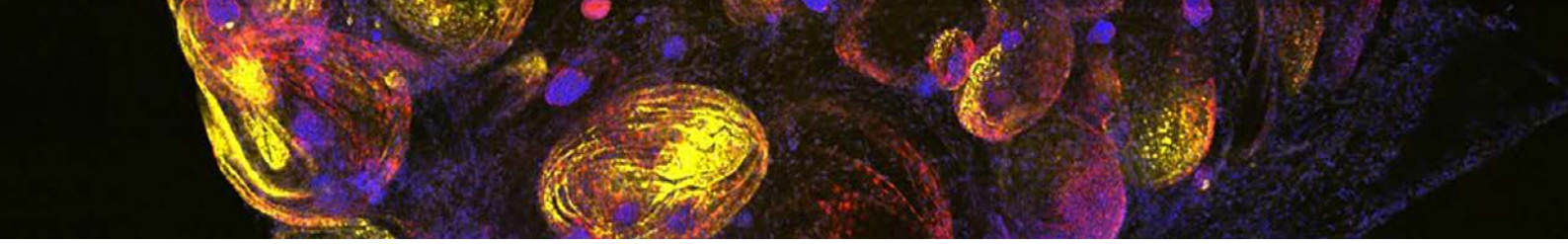
P2

Direct differentiation to generate functional stroma to enrich tissue microenvironment in human kidney organoid

Mengmei Zhu, Chao Zhang, Ximing Gong, Meng Liu, Huamin Wang, Tian Zhang, Yixuan Wang, Yan Li, Jevon Aaron Lesmana, Yun Xia

Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

Generation of a functional human kidney in vitro is the ultimate goal for future replacement therapy. Despite significant advancements, current kidney organoids face several limitations. Nephron organoids contain many nephron-like structures, but lack inter-nephron connectivity. Ureteric bud/collecting duct organoids exhibit extensive branching but are devoid of nephrons. Combining these two types of organoids results in limited nephron-collecting duct connectivity, falling short of recapitulating the organotypic kidney structure observed in vivo, where multiple branched collecting ducts connect to radially arranged nephrons. To achieve this complex architecture in vitro, the inclusion of the third precursor population, stromal progenitors, is essential. The orchestrated interaction among stromal, nephron, and ureteric epithelium progenitors within the nephrogenic niche is pivotal for kidney development. Although stromal cells are present in current organoids, they may represent off-target cells arising during differentiation. Therefore, the objective of this project is to develop a precise stromal progenitor differentiation protocol and then re-establish a close-to-native nephrogenic niche alongside human PSC-derived metanephric mesenchyme (MM) and ureteric bud (UB). Ultimately, this approach aims to generate an organotypic "higher-order structure" kidney organoid in vitro.



P3

FOXM1-MYB and IQGAP3 regulatory network induce dedifferentiated chief cell expansion via activation of MYC in stomach

Junichi Matsuo[1], Takaomi Sanda[1,2], Mitsuhiro Shimura[1,3], Jungwon Lee[1], Nawaphat Jangphattananont[1], Wei Peng Yong[1,4], Linda Shyue Huey Chuang[1], Yoshiaki Ito[1]

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The stomach is regularly exposed to hazardous materials which induce tissue damage. We previously identified scaffold protein IQGAP3 as a proliferating stem cell factor. IQGAP3 is rapidly and robustly induced upon tissue damage. Nevertheless, the molecular mechanism for IQGAP3 induction and its role in tissue repair have been unclear. Here, transcriptome analysis with mice gastric glands showed induction of FOXM1, b-MYB and IQGAP3 in dedifferentiated chief cells of damaged stomach. Mechanistic analysis revealed the interaction of FOXM1 and b-MYB with the IQGAP3 promoter, suggesting FOXM1 and b-MYC work as trans-activators for IQGAP3 during tissue repair. To examine the role of IQGAP3 in stem cell activity in tissue repair, we developed a stomach epithelium-specific IQGAP3 conditional knockout mouse. Attenuation of IQGAP3 expression in the mouse stomach led to impaired tissue repair and suppressed MYC pathway activity. Furthermore, stem cell and mitosis-related genes were also downregulated in the IQGAP3-depleted mice stomach, suggesting that IQGAP3-MYC axis regulates stem cell expansion. Using cell lines, we confirmed that MYC phosphorylation was regulated via the interaction of IQGAP3 with MYC. These findings clarify that FOXM1-MYB/IQGAP3/MYC axis regulates stem cell expansion as a tissue repair process. Induction of IQGAP3 in tissue might contribute to effective tissue regeneration.

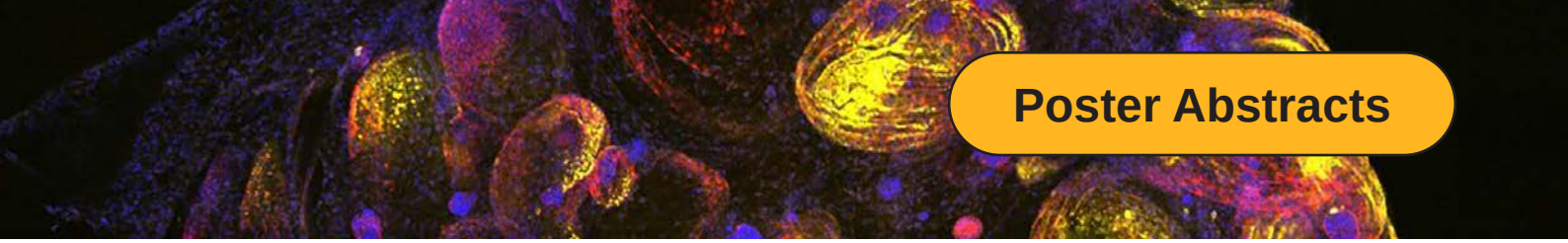
P4

An integrated transcriptomic cell atlas of human kidney organoids

Meng Liu, Lingyi Zhuang, Yun Xia

Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

Kidney organoids derived from human pluripotent stem cells hold great promise for modeling renal development, disease mechanisms, and therapeutic testing. However, protocol heterogeneity and limited benchmarks hinder cross-study comparisons and translational applications. To address this, we constructed a comprehensive single-cell transcriptomic atlas by integrating over 100 datasets from more than 40 independent kidney organoid studies, encompassing over 800,000 cells. This atlas maps organoid-derived cell types onto human fetal and adult kidney references, enabling systematic evaluation of nephron segment identity, maturation state, and protocol fidelity. Beyond benchmarking, the atlas serves as a predictive tool for disease modeling: we demonstrate its utility by analyzing organoid models of polycystic kidney disease and renal fibrosis, identifying both shared and unique transcriptional programs relevant to pathogenesis. The kidney organoid atlas thus provides a unified framework to assess organoid quality, guide protocol optimization, and predict disease-associated transcriptional states, accelerating the development of physiologically and clinically relevant kidney models.



Poster Abstracts

P5

Modelling ischemia reperfusion in human multicellular 3D cardiac microtissue

Rujie Qi[1,2], Roger Foo[1,2], Mathew Andrew Ackers-Johnson[1,2]

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Ischemia–reperfusion (IR) injury involves intricate multicellular interactions within the heart, posing challenges for faithful in vitro modeling. To address this, we developed a three-dimensional (3D) human cardiac microtissue platform comprising four stem cell-derived cell types: cardiomyocytes (CMs), cardiac fibroblasts (CFs), endothelial cells (ECs), and macrophages (Mϕ). Inclusion of non-CM populations promoted CM maturation and enabled stromal–immune cross-talk, thereby supporting the study of coordinated injury responses. Exposure to hypoxia followed by reperfusion induced a distinct ischemic zone characterized by surface-localized cell death, closely resembling in vivo pathology. Notably, the model reproduced responses observed in vivo but absent in 2D culture; for example, periostin (POSTN) expression was strongly induced by TGF-β treatment in 3D microtissues but not in 2D monolayers. The primary objective is to establish a physiologically relevant platform to interrogate IR biology, including the role of candidate genes such as midkine (MDK). Beyond mechanistic studies, the system is well suited for high-throughput drug screening and evaluation of therapeutic interventions, underscoring the translational potential of 3D multicellular cardiac microtissues.

P6

Esrrb loss disrupts the balance between epiblast- and primitive endoderm (PrE)-like cell fate during the expanded-to-naïve transitive process

Nadia Omega Cipta, Yingying Zeng, Ka Wai Wong, Yuin-Han Loh

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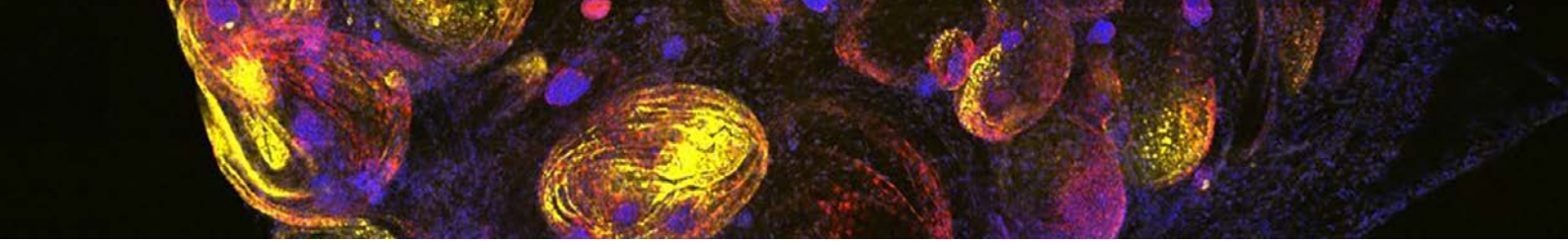
Although crucial in the naïve embryonic stem cells, we previously reported that the regulatory role of Esrrb was limited in the expanded potential stem cell (EPSC) state. In this study, we studied the role of Esrrb in the context of exit from expanded potency. In an expanded-to-naïve transition assay, loss of Esrrb skewed the EPSC's differentiation preference towards primitive-endoderm (PrE) fate. This was marked by increased PrE genes and upregulation of transposable elements with unreported roles in PrE (RLTR1B and RMER16). The increased number of these PrE-like cells contributed to enhanced blastoid production in a blastoid formation assay. Studies have reported that Esrrb is beneficial for inducing extraembryonic endoderm (XEN), an in-vitro model for PrE, from pluripotent ESC or fibroblast. Our findings offered another angle, in which a PrE-like state is induced from a totipotent-like state (EPSC).



P7

Functional analysis of FOXG1 in human thymus and epidermal stem cells fate

Jun-Ichi Sakabe[1,2], Chan Wing Yue[1], Alvin Chua[1,2], Keya Roy[1], Bien Keem Tan[1,2] and Barrandon Yann[2]

[1]Department of Plastic, Reconstructive & Aesthetic Surgery, Singapore General Hospital, Singapore; [2]Musculoskeletal Sciences, Academic Clinical Programmes, Duke-NUS Medical School, Singapore

We previously reported that rat epithelial stem cells of non-cutaneous origin—including those from the cornea, esophagus, vagina, bladder, prostate, and thymus—expressing the transcription factor Tp63, a master regulator of epidermal and skin appendage development, can respond to morphogenetic signals and cross lineage boundaries. In a skin microenvironment, these cells generate epidermis, hair follicles, and sebaceous glands. Among them, we showed that thymic epithelial cells (TECs) are specifically expressing FOXG1, a transcription factor essential for neural development. Notably, human TECs (hTECs) express some genes associated with epithelial stratification, particularly within Hassall's bodies, although their precise role remains unclear. Our clonal analyses identified several sub-populations of hTEC stem cells, among which one expresses a number of genes involved in epidermal stratification, although the latter cannot form a fully differentiated self-renewing epidermal keratinocytes. A key distinction between hTECs and human epidermal keratinocyte stem cells (hEKs) is the exclusive expression of FOXG1 in hTECs. Therefore, we hypothesize that FOXG1 governs lineage restriction between thymic and epidermal fates. To test this, we performed functional assays involving FOXG1 upregulation and downregulation in both cell types. These studies aim to elucidate how FOXG1 modulates gene expression and cell dynamics, providing novel insight into the developmental plasticity shared by thymic epithelia and epidermis.

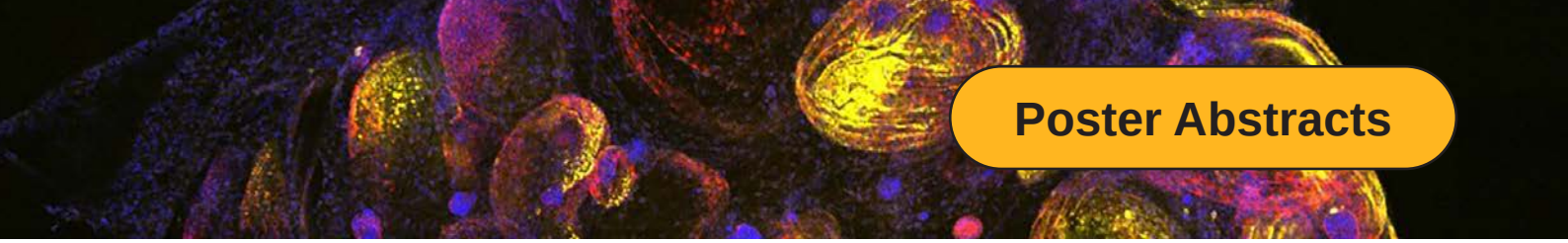
P8

Investigating microglial contributions to Amyotrophic Lateral Sclerosis (ALS) using immuno-competent organoids

Shiying Liu[1], Stephanie Howe[2], Satish Kumar Tiwari[3], Hang Xu[4], Florent Ginhoux[3], Shyuan Ngo[2], Jinmiao Chen[4], Shi Yan Ng[1]

*[1]Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore; [2]Australian Institute for Bioengineering and Nanotechnology, The University of Queensland; [3]Singapore Immunology Network (SIgN), Agency for Science, Technology and Research (A*STAR), Singapore; [4]Bioinformatics Institute, Agency for Science, Technology and Research, (A*STAR), Singaporee*

Spinal cord organoids derived from induced pluripotent stem cells (iPSCs) offer a powerful platform for investigating incurable neurodegenerative diseases like Amyotrophic Lateral Sclerosis (ALS), which causes degeneration of the motor neuron. However, a major limitation has been the absence of microglia, the CNS-resident immune cells increasingly recognized as active contributors to ALS pathogenesis. To address this, we generate chimeric immuno-competent spinal organoids by co-culturing iPSCs-derived microglia (iMac) with spinal organoids (Org) using isogenic pairs of iPSCs with and without the heterozygous TDP43G298S mutation, including OrgWTiMacWT, OrgWT iMacG298S, OrgG298SiMacWT, OrgG298S iMacG298S. Comparing between OrgWTiMacWT and OrgG298S iMacG298S, we observed increased phosphorylation and cytoplasmic mislocalization of TDP43 in the latter, mimicking TDP43 proteinopathy frequently seen in ALS patients. Culture of ALS microglia with WT organoids (OrgWTiMacG298S) induces TDP43 proteinopathy in motor neurons. These MNs show reduced expression of axon guidance and neurotransmission markers, indicative of possible neuronal "dying-back", implying ALS microglia may drive spinal cord organoid to ALS phenotype. Culture of WT microglia with ALS organoids (OrgG298SiMacWT) appears to reduce TDP43 phosphorylation and mislocalization, as well as reduce pro-inflammatory marker expression, indicating WT iMACs may rescue the ALS phenotype in spinal cord organoid.



Poster Abstracts

P9

Identification of key maturation genes during nk cell differentiation from CB-HSPCs using clonal and lineage tracing

Pongsatorn Horcharoensuk[1,2], Uma Sangumathi Kamaraj[2], Nadia Omega Cipta[2], Tang Shin Yi[2], Hu Li4, Qi-Jing Li[1,3], Reshma Taneja[1], Yuin-Han Loh[2]

[1]Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; *[2]Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore*; *[3]Singapore Immunology Network (SIgN), Agency for Science, Technology and Research (A*STAR), Singapore*; *[4]Department of Molecular Pharmacology & Experimental Therapeutics, Mayo Clinic, Rochester, MN, USA*

Cord blood–derived hematopoietic stem and progenitor cells (CB-HSPCs) represent a promising source of natural killer (NK) cells for cancer immunotherapy. However, the current differentiation protocols often yield immature NK cells with limited cytotoxicity. The clonal dynamics underlying NK development during ex vivo differentiation also remain poorly defined. Here, we combined lineage tracing with single-cell transcriptomics to dissect molecular programs regulating NK cell differentiation, maturation, and function across feeder-free and feeder-dependent platforms. We identified three predominant NK subsets including conventional NK (cNK) cells, innate lymphoid cell 3 (ILC3)-like NK cells, and myeloid-like NK cells. Clonal lineage tracing revealed that feeder-free and OP9 systems favored ILC3-like differentiation, while OP9-DL1 co-culture strongly promoted cNK lineage commitment. Trajectory analysis of clonal datasets, coupled with in silico perturbation, identified key regulators of NK maturation, including Gene X/Y. Pharmacological targeting with drug A and drug B enhanced NK maturation and cytotoxic activity. Together, our study maps the clonal and transcriptional landscape of NK cell development from CB-HSPCs and highlights molecular regulators that can be leveraged to improve NK-based immunotherapy.

P10

Cranial placode differentiation defects in individuals born without a nose

Vanitha Venkoba Rao[1], Xinran Ji[1], Jasmine Yi Ying Heng[1], Frederique Magdinier[2], Bruno Reversade[3], Shifeng Xue[1]

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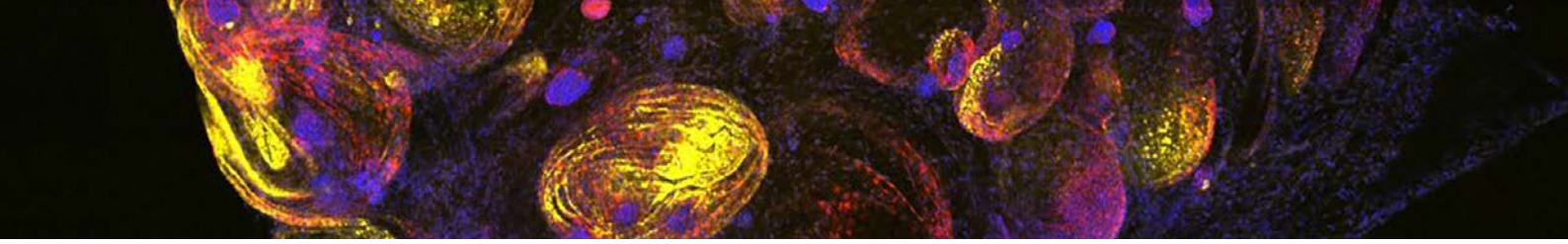
Bosma arhinia microphthalmia syndrome (BAMS) is congenital disorder characterized by the absence of a nose, along with eye and reproductive anomalies. BAMS is caused by heterozygous missense variants in SMCHD1, an epigenetic regulator. Despite uncovering the genetic basis of BAMS, the cellular basis of the disease has remained elusive. The embryonic development of the nose involves direct contributions from both the neural crest and cranial placodes. Here we differentiated patient iPSCs towards the cranial placode lineage and found that they exhibited significant differentiation defects. A combined transcriptome and methylome analyses revealed a patent dysregulation in cell adhesion but without overt apoptosis. Together our research suggests that BAMS is caused by impaired differentiation to cranial placode cells and changes in cell adhesion, offering new insights into the cellular pathology of this enigmatic syndrome.s



P11

Fisetin attenuates human macrophage polarization and pro-inflammatory responses via NF-kB pathway and lipid accumulation

Nattaya Damkham[1], Chanchao Lorthongpanich[1], Pakpoom Kheolamai[2,3], Surapol Issaragrisil[4]

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Natural anti-inflammatory compounds are gaining recognition as promising therapeutic agents due to their lower adverse effects compared with conventional drugs. Fisetin, a dietary bioflavonol found in fruits and vegetables, has shown anti-inflammatory activity in mouse macrophages, but its effects on human macrophages remain unclear. Here, we investigated the anti-inflammatory effects of fisetin in human monocyte-derived M1 macrophages. THP-1 cells and primary human monocytes were derived into M1 macrophages followed by fisetin pre-treatment. Our results shown that Fisetin significantly reduced the production and secretion of pro-inflammatory cytokines (IL-6, TNF-α, IL-1β, IL-8) and chemokines (MCP-1, CCL5, CXCL9, CXCL10), while also suppressing NLRP3 inflammasome expression, reactive oxygen species production, phagocytic activity, and lipid accumulation. The anti-inflammatory effects of fisetin were mediated, at least in parts, by suppression of the NF-κB signaling pathways. These findings demonstrate that fisetin attenuates M1 macrophage polarization and inflammatory responses through NF-κB suppression and lipid accumulation. The knowledge gained from this study provide critical insights into the anti-inflammatory effects of fisetin in human pro-inflammatory M1 macrophages and highlight its potential as a clinically relevant therapeutic agent for managing chronic inflammatory diseases, including atherosclerosis, neurodegeneration, and inflammatory bowel disease.

P12

Chronic palmitate impairs beta cell GSIS via calcium dysregulation

Shiru Qin[1,2], Si Rong Heng[1], Carmen Ching[1,3], Wu Jiayee[4], Jayantha Gunaratne[4,5], and Adrian Kee Keong Teo[1,2,3,6]

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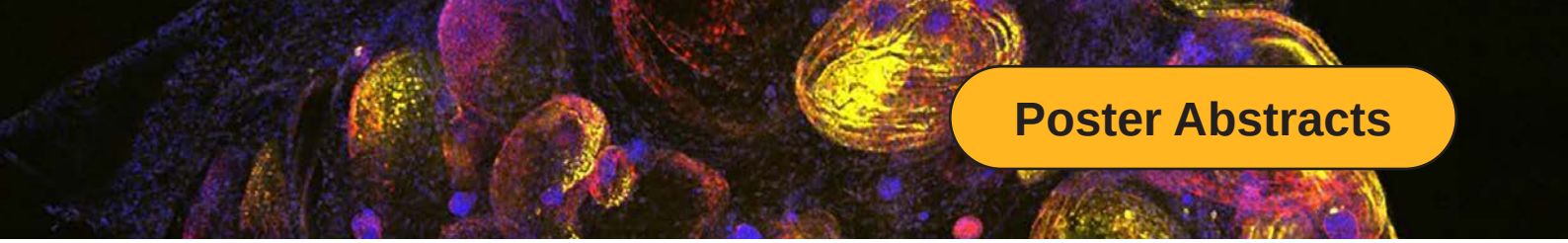
Diabetes is characterised by chronic hyperglycemia resulting from impaired insulin secretion or reduced cellular responsiveness to insulin. Lipotoxicity has been implicated in progressive beta cell dysfunction, with palmitate commonly used as an in vitro model to investigate its direct effects. Acute palmitate exposure has been reported to enhance insulin secretion in isolated human islets, whereas chronic exposure reduces insulin release. The underlying mechanisms regulating insulin secretion under sustained lipotoxic stress remain poorly understood. Here, we exposed EndoC-βH1 cells to a week-long palmitate treatment to model chronic lipid exposure. This resulted in disrupted ER–mitochondrial calcium coupling, characterised by enhanced ER calcium release and activation of compensatory ER stress responses. These changes were accompanied by reduced phosphorylation of regulators involved in calcium transfer, protein folding, and stimulus–secretion coupling. The resulting imbalance between ER calcium release and mitochondrial calcium uptake likely diminished mitochondrial ATP generation and impaired calcium-dependent exocytosis, leading to impaired glucose-stimulated insulin secretion. These findings provide mechanistic insights into how chronic palmitate exposure perturbs calcium homeostasis and beta cell function, offering a potential link between lipotoxicity and the progressive beta cell dysfunction observed in type 2 diabetes.



Poster Abstracts

P13

Identifying novel drivers of cardiac lineage specification and cardiomyocyte maturation using paired short/long-read scRNA-seq

Ryan Fan Ruiming[1], Elaine Cao[2], Aneesh[1], Faith Ong[1], Jay W Shin[2], Roger Foo Sik Yin[1,3]

*[1]National University of Singapore, Department of Medicine; [2]A*STAR, Genome Institute of Singapore, [3]A*STAR, Institute of Molecular Cell Biology*

Alternative splicing – the process by which genes encode different isoforms – allows for greater phenotypic diversity at the cellular level. Isoforms are prominent in every aspect of biology, but their complex patterns of regulation have not been comprehensively decoded due to the limitations of short-read sequencing. However, the combination of single-cell RNA sequencing (scRNA-seq) with long-read technologies provides a powerful platform, permitting the study of isoform expression patterns whilst decoding cellular heterogeneity and cell state transitions. Leveraging these advantages, we examined the transcriptomes of important stages in cardiomyocyte development using paired short/long-read sequencing to identify novel drivers of cardiac lineage specification and cardiomyocyte maturation. Here we report the detection of 33,602 genes and 96,816 isoforms across 28,477 single cells representative of different timepoints during directed cardiomyocyte differentiation (D0, D3, D7, D20, D48). Distinct cardiomyocyte cell states were identified, and through integrative analysis with public datasets, we shortlisted novel candidates that may be key modulators or effectors of cardiac specification and maturation. Furthermore, we show remarkable differences between clustering at the gene- and transcript-level that highlights significant epigenetic regulation of cardiac isoforms, and explore differential transcript usage across cardiomyocyte regulatory networks.

P14

Engineered U1-snRNA restores ABCA4 expression in phenotypically relevant in vitro retinal disease models for Stargardt

Animesh Banerjee[1], Paolo Pigini[2], Wang Chao[6], Wendy Wong[5], Bhav H Parikh[1], Kanaga Sabapathy[1,6], Dave Keng Boon Wee[1], Xinyi Su [1,3,4,5]

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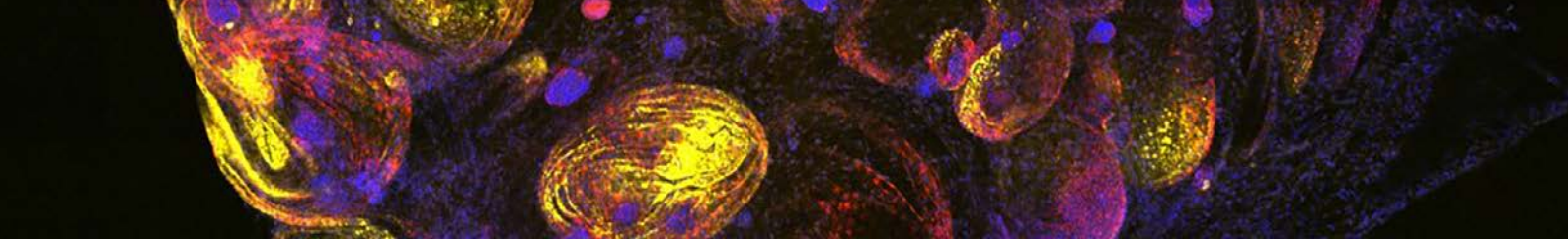
RNA-based therapeutics are rapidly emerging as a promising approach for inherited diseases. However, current methods have some technical barriers, such as antisense oligonucleotides, which often require significant chemical modifications to be effective, and CRISPR-based editors can trigger immune responses. A different approach is to use engineered U1 small nuclear RNAs (U1snRNAs), which are naturally present in cells and can be modified to correct abnormal splicing. Although promising, this strategy has barely been explored for retinal diseases, where splicing mutations are a significant cause of vision loss. In this study, we investigated U1snRNA-based therapies for Stargardt disease (STGD1), a common inherited macular degenerative disease primarily caused by mutations in the ABCA4 gene. To enable therapeutic testing, we first established phenotypically relevant retinal in vitro models using patient-specific iPSC-derived retinal pigment epithelial (iRPE) cells (2D) and retinal organoids (3D) that carry ABCA4 mutations. Both 2D and 3D models retained native retinal identity and stably expressed the mutant ABCA4 transcript. Pathological hallmarks of STGD1, such as intracellular lipid accumulation, became evident by six weeks, mimicking the progressive disease features. Mutation-matched engineered U1snRNAs successfully restored wild-type ABCA4 transcript levels in iRPE cells and reduced lipid accumulation, demonstrating both molecular and functional rescue. Together, this study establishes engineered U1snRNA as a compelling RNA therapeutic modality for ABCA4-associated retinal disease. Further, we also provide robust lab-grown retinal disease models that can be used to test and refine splicing-corrective therapies for inherited retinal disorders.



P15

Spatial cartography of human thymus enables the geopositioning of lineage transcription factors in rare mimetic thymic epithelial cells

Uma Sangumathi Kamaraj[1], Ying Chen[1], Junjie Lei[1], Pradeep Gautam[1], Pongsatorn Horcharoensuk[1,2], Czaryna K M Clemente[3], Katja G. Weinacht[4], Nicholas R J Gascoigne[5], Jinmiao Chen[6], Ching Kit Chen[3], Qingfeng Chen[1,6], Qi-Jing Li[1,6], Lai Guan Ng[7], Yuin-Han Loh[1,2,8,9]

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The thymus is the primary site for T cell maturation, but a detailed high-resolution spatial atlas is needed to identify rare cell types and understand their microenvironment. In our study, we employed Stereo-seq spatial transcriptomics to generate a comprehensive spatial map of the human fetal and pediatric thymus, analyzing samples from the second trimester (13 to 18 weeks post-conception) and early childhood (7 weeks to 6 years). Our results reveal the thymus's spatial organization, including distinct regions such as the outer cortex, inner medulla, and septa. We identified diverse cellular niches composed of thymic epithelial cells (TECs), thymocytes, and immune cells like dendritic cells, macrophages, and B cells. By integrating transcriptomic and proteomic data, we discovered lineage-defining transcription factors, including mimetic TFs (mimeTFs), that regulate rare TEC populations. Additionally, we identified novel transcription factors potentially involved in these regulatory processes. Our spatial atlas provides valuable insights into thymic architecture, cellular diversity, and mechanisms regulating T cell development.

P16

BMP signaling modulates human cortical expansion and maturation

Dongliang Ma[1#*], Jiaen Lin[1#], Qiannan Deng[1¥], Anselm S. Vincent[1], Jing Guo[2], Yiping Fan[3], Mahekta R. Gujar[1], Suresh Divya[1], Wai Hon Chooi[1], Edwin Shepherdson[3], Saumya S. Jamuar[4], Jerry Kok Yen Chan[5], Enrico Petretto[2], and Hongyan Wang[1,4,6*§]

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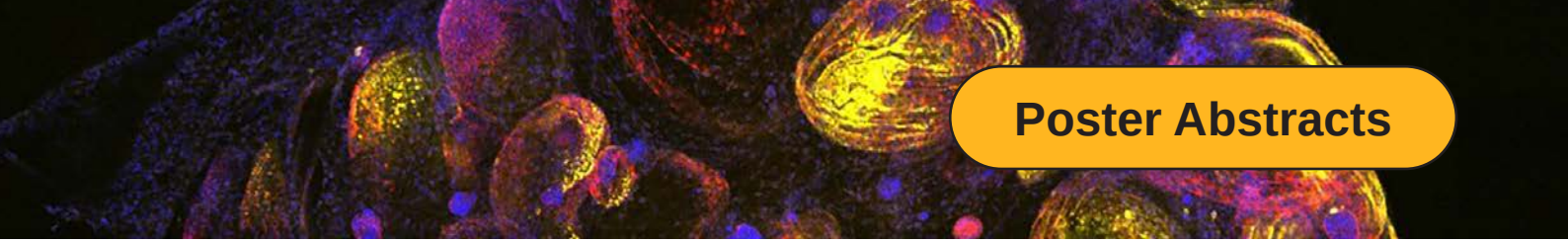
Outer radial glia (oRG) cells, a stem cell population enriched in the developing neocortex of primates, including humans, are essential for neocortical expansion. However, little is known about molecular mechanisms underlying the generation and differentiation of oRG cells. Here, we demonstrate that BMP signaling enhances oRG expansion and astrocyte differentiation in human cerebral organoids. These effects are validated using cortical slices derived from primary human fetal brain tissues. BMP4 treatment activates SMAD1, resulting in the upregulation of oRG and astrocyte markers. Single-cell RNA sequencing, trajectory analysis, and gene regulatory network analysis have identified distinct BMP4-driven transcriptional hierarchies underlying oRG expansion. Ultimately, BMP signaling activation enhances neuronal activity and maturation of the human cerebral organoids. BMP4-treated organoids likely offer a more mature and physiologically relevant platform for modeling neurodevelopment and related brain disorders.



Poster Abstracts

P17

Cell therapy cryogenics: Moving beyond the DMSO era

Steve Oh[1], Simon Cool[2], Alan Lam[2], Arthi Shridhar[1], Xiaoxi Wei[1]

*[1]X-Therma Inc., USA; [2]A*STAR, Singapore*

Cryopreservation remains a critical bottleneck in cell and gene therapy (CGT) manufacturing, where dimethyl sulfoxide (DMSO) continues to impose cytotoxic, variable, and process-unfriendly limitations. We evaluated XT-Thrive®, a chemically defined, DMSO-free, non-toxic cryopreservation solution designed to improve viability and functionality of mesenchymal stromal cells (MSCs) and T cells across cell banking and therapeutic applications. Using patient-derived MSCs expanded in serum-free and serum-containing conditions, XT-Thrive® preserved up to 30% higher post-thaw viability compared to the clinical GMP standard (CS10) and maintained superior growth and clonogenic potential during microcarrier culture. Cells cryopreserved with XT-Thrive® exhibited normal karyotype stability, sustained tri-lineage differentiation, and absence of tumorigenic transformation. In CAR T-cell studies, XT-Thrive® retained cytotoxic function, IL-2 secretion and immunophenotypic integrity post-thaw, supporting use in adoptive immunotherapy workflows. XT-Thrive® demonstrated excellent tolerability following localized foot pad injections in rodents, with minimal edema and compared to DMSO-containing controls. Fresh-never-frozen storage with XT-NoVo® alleviates the cryochain burden and prevents freeze-related injury. Also DMSO-free, subzero preservation solution, enables the safe and effective short-term storage of cryo-sensitive cells and tissues with limited logistical hurdles. Collectively, these results position X-Therma's platform as a next-generation, DMSO-free preservation solution spanning cells to organs, enabling safer, more reliable, and accessible therapies.

P18

Orangutan naïve iPSCs recapitulate early zygotic genome activation in vitro

Xin Gao, Yuin-Han Loh

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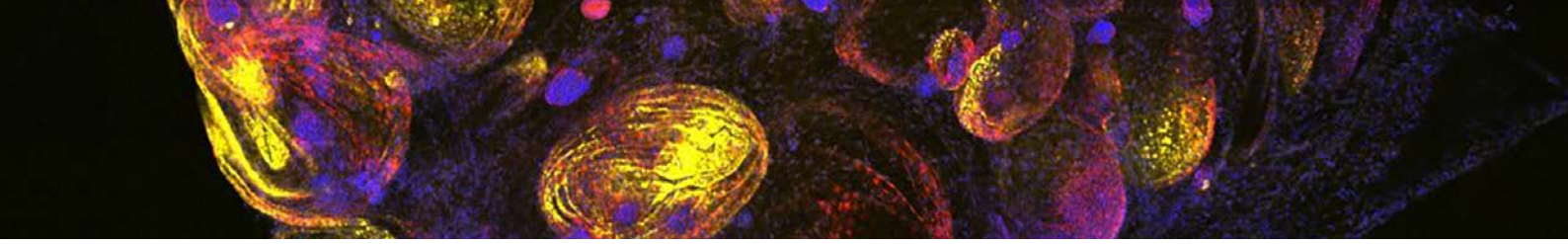
Pluripotent stem cells can exist in different states, reflecting distinct developmental potentials. In this study, we attempted to convert orangutan induced pluripotent stem cells (iPSCs) from a primed to a naïve state. Following the conversion, we identified a subpopulation of cells exhibiting high expression of zygotic genome activation (ZGA) genes, suggesting the acquisition of early embryonic-like transcriptional features. These findings provide a platform for studying early primate embryogenesis and offer insights into the molecular characteristics associated with pluripotency state transitions in great apes.



P19

Identification of potential regulators crucial for thymic epithelial cell development via small-molecule screening

Ying Chen, Yang Kai Ng, Yuin-Han Loh

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Thymic epithelial cells (TECs) are one of the primary stromal cell types present responsible for T-cell development and maturation. During human thymic involution, TECs seem to decrease in numbers, which are associated with the evident atrophy observed. While the underlying mechanism remains debatable, recent research has started to focus on possible strategies for regeneration of TECs. Here, we presented a screening-based workflow in combination with in-vitro TEC differentiation protocol. The aim is to unbiasedly identify any potential pathway or molecular target that could be important for TEP differentiation. Based on our preliminary pilot test, we identified two potential pathways which further induced the expression of a pan-TEC marker KRT5. In the future, we will expand our screening to a larger chemical library.

P20

Exploring the effect of lipid dysregulation and neuroinflammation in ALS astrocytes

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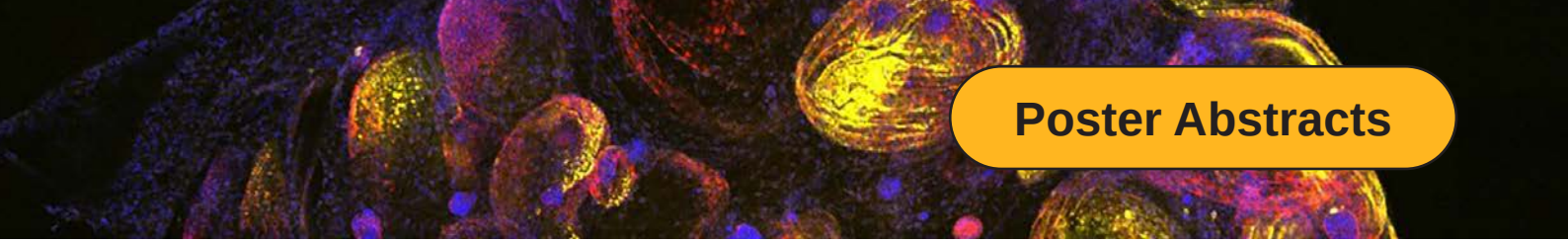
Astrocytes are the most abundant glial cells in the central nerve system, crucial for supporting neuronal health and brain homeostasis. However, increasing evidence shows that their secretory profile contributes to astrocyte-mediated toxicity. Although astrocytes secrete pro-inflammatory cytokines attributing to neuronal death, the full extent of neurodegenerative phenotypes has not been captured. Recent studies highlight that lipid dysregulation has emerged as a major risk factor for many neurodegenerative diseases, including Alzheimer's disease, and Amyotrophic Lateral Sclerosis (ALS). Given their role as highly secretory cells managing lipid storage and metabolism, astrocytes have garnered attention. Here, we use ALS as an example of neurodegenerative disease to investigate lipid metabolic defects in hiPSC-derived spinal astrocytes and their impact on motor neuron function and disease progression. Our study advanced existing methods, reducing differentiation time of hiPSCs into spinal astrocytes to 30 days. Lipidomic analysis uncovered an increase in omega-6 fatty acids, especially arachidonic acid (AA). Our findings highlight the link between neuroinflammation and lipid dysregulation in the ALS spinal cord. We aim to elucidate potential mechanisms by which astrocyte-mediated lipid dysregulation accelerates ALS progression. Collectively, this study advances our understanding of astrocyte contributions to neurodegeneration and highlights potential disease biomarkers and therapeutic targets in ALS.



Poster Abstracts

P21

A rare craniofacial disorder caused by LINE1-driven losses of a distal *ALX1* enhancer cluster

Navin Brian Ramakrishna[1], Umar B Mohamad Sahari[1], Hülya Kayserili[2], Arda Çetinkaya[3], Nurten Akarsu[3], Jay W Shin[1], Bruno Reversade[1, 4], et al.

*[1]A*STAR Genome Institute of Singapore, Singapore; [2]KOC University, Turkïye; [3]Hacettepe University, Turkïye; [4]KAUST, Saudi Arabia*

Facial malformations affect a third of congenital disorders, with defects originating in progenitor facial cells. We identified individuals from independent consanguineous families with a rare facial disorder characterised by a large cleft and eye defects, phenocopying the recessive Frontonasal Dysplasia 3. However, the causative gene - homeodomain transcription factor *ALX1* - was not mutated. Instead, via long-read sequencing, we identify large, overlapping deletions distal to *ALX1*. The deletions span a putative enhancer cluster during a transient window of facial precursor development from reanalysis of craniofacial epigenetic datasets, thus representing a novel craniofacial enhanceropathy. Here, I will describe our investigation in further epigenomic profiling and functional interrogation of the enhancer cluster impacting *ALX1* gene expression, leveraging a differentiation model of human craniofacial neural crest cells from hPSCs, using patient-derived iPSCs, CRISPR/a/i enhancer-perturbed hESCs, as well as animal modelling. We additionally show the remarkable contribution of sequence diversity in this cluster in more common variation among human faces and in evolution. I end with insights into the etymology of the identified large structural variants which share hallmarks of transposable element non-allelic homologous recombination events, and link this type of vulnerability over putative enhancer regions to cognate promoters of other craniofacial-associated genes.

P22

A scaffold-free human 4-cell-type cardiac microtissue model for investigating metabolic stress-induced heart failure

Khe Ying Chong[1], Chang Jie Mick Lee[1,2], Roger S.-Y. Foo[1,2]

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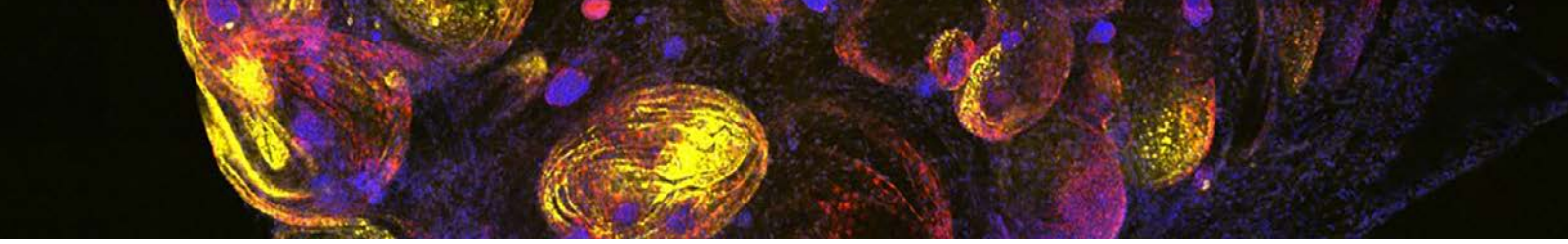
In Asia, nearly two-thirds of heart failure (HF) patients present with multimorbidities, yet the mechanisms underlying metabolic stress–induced HF remain poorly defined. There is therefore a pressing need for human-based models that recapitulate disease pathology and support high-throughput drug discovery. In this study, we adapted an existing cardiac microtissue model by incorporating macrophages to capture the immune signature of HF, generating a four-cell-type cardiac microtissue (4CT-MT) comprising the major cardiac cell types. To mimic metabolic stress, 4CT-MT was exposed to a high-fat, high-sugar, pro-inflammatory cocktail consisting of glucose, palmitic acid, oleic acid, interferon-gamma and angiotensin II. This model successfully reproduced some key hallmarks of heart failure with preserved ejection fraction (HFpEF), including cardiomyocyte hypertrophy, activated inflammatory signaling, and reduced bioenergetics. Additionally, insulin resistance marked by elevated IRS1-Ser307 phosphorylation and impaired relaxation was also observed, suggesting diastolic dysfunction and metabolic derangement. Transcriptomic profiling by bulk RNA-seq revealed downregulation of oxidative phosphorylation and cardiac muscle contraction, coupled with upregulation of immune response. Collectively, the metabolic stress–induced 4CT-MT provides a more physiologically relevant platform recapitulating the cardiac immune function, to investigate the interplay between myocytes and non-myocytes in HF progression.



P23

Histone deacetylase HDAC4 promotes neural stem cell reactivation in Drosophila

Yang Gao, Jiaen Lin, Amanda Ng Yunn Ee, and Hongyan Wang

Neuroscience and Behavioral Disorders Programme, Duke-NUS Medical School, Singapore

A delicate balance between quiescent and proliferative states of neural stem cells (NSCs) is essential for neurogenesis, brain development and homeostasis. Dysregulation of NSC reactivation is associated with neurodevelopmental and neuropsychiatric disorders. Histone deacetylase 4 (HDAC4) variants are identified in patients with neurodevelopmental disorders. However, current studies focus on its implication in neurodegenerative diseases, because HDAC4 promotes aggregation of Huntingtin protein. The role of HDAC4 during brain development remains unclear. We find that HDAC4 is highly expressed in the developing brain in both vertebrates and invertebrates. We further demonstrate that HDAC4 plays a crucial role in NSC reactivation and brain development in Drosophila. HDAC4 expression levels in NSCs increase along with their reactivation. Depletion of HDAC4 results in notable defects in NSC reactivation and brain development. In contrast, HDAC4 overexpression leads to premature reactivation of NSCs. We show that HDAC4 undergoes SUMO modification, which enhances its protein stability, thereby facilitating NSC reactivation. Moreover, HDAC4 genetically interacts with the Hippo pathway during NSC reactivation. Inhibition of the Hippo pathway effectively restores the NSC reactivation defects induced by HDAC4 depletion. In conclusion, our study uncovers a pivotal role for HDAC4 in Drosophila NSC reactivation and brain development through inhibiting the hippo pathway

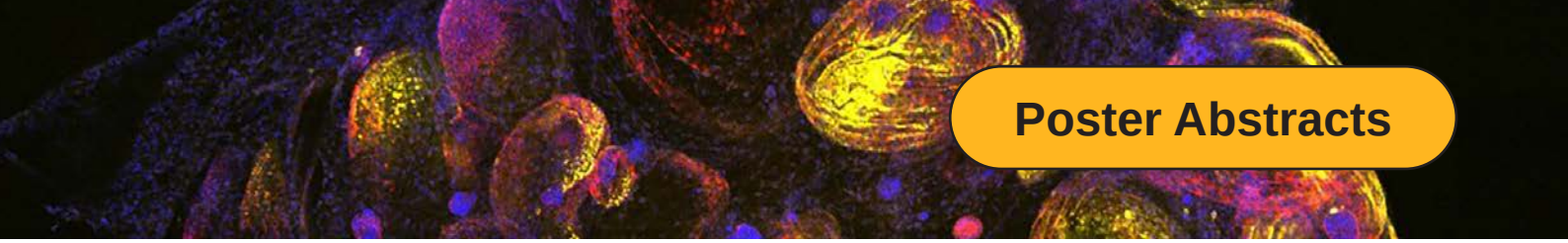
P24

Engineered synthetic polymers modulate fibrotic responses in stem cell-derived retinal pigment epithelium: Toward non-pharmacological strategies for proliferative vitreoretinopathy prevention

Rajvinder Singh Khare[1], Qianyu Lin[2], Asfa Alli Shaik[3], Bhav Harshad Parikh[3], Jason YC Lim[2,4], Xian Jun Loh[2,5], Xinyi Su[1,3,6]

*[1]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [2]Institute of Materials Research and Engineering (IMRE), Agency for Science, Technology and Research (A*STAR), Singapore; [3]Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore; [4]Department of Materials Science and Engineering, National University of Singapore, Singapore; [5]Department of Material Science and Engineering, Nayang Technological University, Singapore;[6]Singapore Eye Research Institute (SERI), Singapore*

Proliferative vitreoretinopathy (PVR) remains a major cause of surgical failure and vision loss following retinal detachment, driven by aberrant wound-healing and fibrotic membrane formation. Retinal pigment epithelium (RPE) cells, when stimulated by pro-fibrotic cytokines, undergo epithelial-mesenchymal transition (EMT) and acquire contractile, myofibroblasts-like properties that contribute to this scarring process. While current clinical strategies lack effective pharmacological interventions for either the prevention or reversal of PVR, emerging biomaterial-based approaches have shown potential to modulate fibrotic responses. In this study, we investigated how specific physiochemical properties of synthetic polymers influence cytokine-induced fibrosis in stem-cell derived RPE cultures. These are random multi-block branched amphiphilic polyurethane copolymer synthesised by coupling PEG, PPG, PCL-diol, and glycerol with hexamethylene diisocyanate (HMDI). We found that polymers characterized by higher glycerol content, shorter average branch length, smaller micelle diameter, and greater monodispersity were significantly associated with reduced formation of fibrotic membranes *in vitro*. Correspondingly, mRNA expression of canonical EMT transcription factors and extracellular matrix proteins was markedly decreased in polymer-exposed RPE under fibrotic stimulation. Collectively, our data support the potential of tailored polymer designs as a novel biomaterial-based approach to prevent fibrotic membrane formation in retinal disease, providing a foundation for future translational applications in PVR management.



Poster Abstracts

P25

Thermogel-mediated dual neurotrophic factor delivery enhances retinal pigment epithelial cell survival

Karishma N Mehta[1], Rubayn Zhi Rong Goh[3], Jason Y. C. Lim[3], Qianyu Lin[3], Yi Jian Boo[3], Bhav Harshad Parikh[1], Daniel Soo Lin Wong[1], Zengping Liu[1,2], Xian Jun Loh[3], Xinyi Su[1,2]

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Age-related macular degeneration (AMD) remains a major cause of irreversible blindness, and while retinal pigment epithelial (RPE) cell transplantation offers promise, graft survival is hindered by oxidative and inflammatory stress. To address this, we developed a thermo-responsive hydrogel platform enabling sustained delivery of neurotrophic factors to support transplanted RPE. Eight candidate polymers were screened for biocompatibility and neurotrophic factor release. Among them, EPC7 showed optimal compatibility with stem cell-derived RPE (SC-RPE) and was well tolerated following intravitreal injection in rabbits. When loaded with brain-derived neurotrophic factor (BDNF) and pigment epithelium-derived factor (PEDF), EPC7 provided controlled dual release for over two months, significantly enhancing SC-RPE viability compared to gel-free cultures. This dual-factor thermogel system thus serves as a promising surgical adjunct to improve RPE graft integration and long-term survival. Ongoing studies are evaluating its efficacy in preclinical models of retinal degeneration.

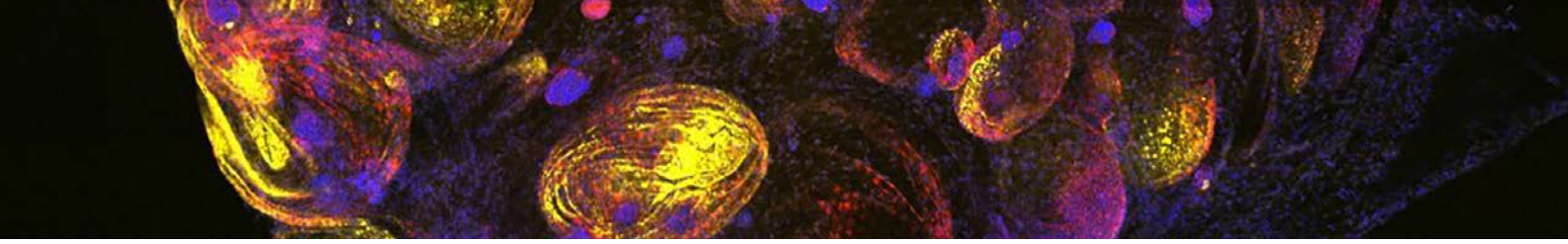
P26

Identifying key regulators of MSC stemness to enhance regenerative therapies

Tong Ming Liu, Yuin-Han Loh, Simon Cool

*Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore*

Although mesenchymal stem cells (MSCs) have been evaluated in more than 1,500 clinical trials for the treatment of over 30 diseases, the molecular mechanisms governing MSC stemness remain poorly defined. Using our proprietary iPSC-to-MSC differentiation platform, we identified two key regulators of MSC stemness: a HOX transcription factor and a BMP antagonist. Knockdown of the HOX transcription factor impaired MSC proliferation, accelerated cellular senescence, and markedly reduced colony-forming unit–fibroblast (CFU-F) formation as well as multi-lineage differentiation. Conversely, HOX overexpression enhanced multi-lineage differentiation in vitro and promoted calcium deposition in vivo. Notably, HOX expression declined during in vitro expansion in parallel with the downregulation of other stemness-associated genes. CUT&Tag and rescue experiments demonstrated that HOX directly regulates Twist1 as an upstream factor. In addition, we also screened a BMP antagonist as another critical regulator of MSC stemness. Silencing of this gene disrupted MSC morphology and proliferation, markedly reduced the expression of stemness-associated genes, and impaired differentiation potential. Together, these findings not only advance the molecular understanding of MSC biology but also establish a foundation for developing MSC-based gene therapy strategies.



P27

Characterising the role of DNAJC18

Vicky Lai[1], Rijan Gurung[1], Chang Jie Mick Lee[1], Matias I. Autio[1], Alexander Bershadsky[2], Roger SY Foo[1]

[1]Medicine, National University of Singapore, Singapore; [2]Mechanobiology Institute, Singapore, National University of Singapore, Singapore

DNAJC18 is a poorly characterized member of the type III HSP40 family. Multi-omic datasets first linked DNAJC18 to dilated cardiomyopathy (DCM) through overlapping eQTL/haQTL signals and GWAS loci. Patient samples also reveal upregulation of DNAJC18 in both myocardial infarction (MI) and DCM. We found that DNAJC18 is most expressed in endothelial cells and is responsive to stress, highlighting its potential role in vascular adaptation. Using CRISPR-Cas9 knockout and rescue approaches in human iPSC-derived endothelial cells, we demonstrate that the loss of DNAJC18 impairs angiogenesis and destabilizes the cytoskeleton. Global transcriptomic and proteomic profiling confirm activation of stress pathways and suppression of angiogenesis-related regulators. To extend these insights, we pioneered a multi cell-type 3D organoid model derived from human pluripotent stem cells, incorporating endothelial cells, cardiomyocytes, macrophages, and fibroblasts. Within this system, DNAJC18 knockout organoids display mitochondrial deficiency, underscoring its essential role in cellular energy homeostasis and tissue-level stress adaptation. Importantly, DNAJC18 is strongly induced by different stressors, suggesting its role as a stress-responsive regulator. This work represents the first functional characterization of DNAJC18 in a stem cell–derived model, highlighting a powerful organoid system, and positions DNAJC18 as a novel candidate for therapeutic targeting in heart disease.

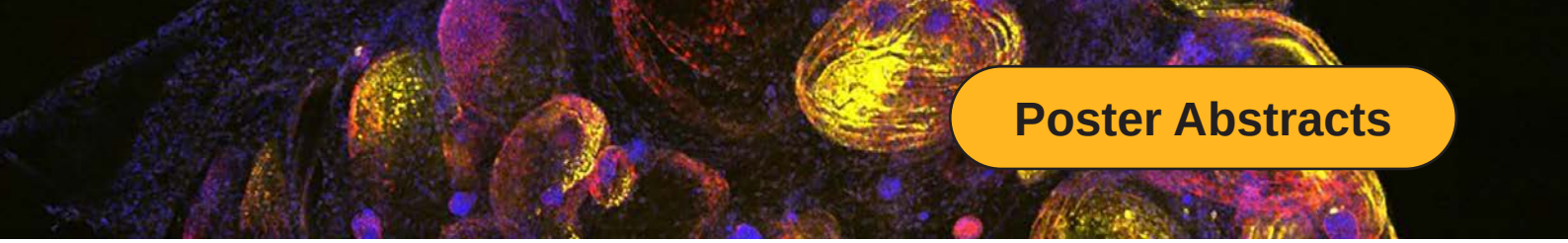
P28

Microproteins Simba1 and Simba2 activate Wingless signaling during the reactivation of neural stem cells in Drosophila

Jiaen Lin[1], Qiannan Deng[1§], Yang Gao[1], Ye Sing Tan[1], Zheng Zhong[2], Lay Keng Angie Tan[2], Boon Ooi Patrick Tan[2], David M. Virshup[2], Justin A. Bosch[3], Norbert Perrimon[4,5], and Hongyan Wang[1,6,7*]

[1]Neuroscience & Behavioral Disorders Programme, Duke-NUS Medical School, Singapore; [2]Cancer & Stem Cell Biology Programme, Duke-NUS Medical School, Singapore; [3]Department of Human Genetics, University of Utah School of Medicine, Salt Lake City, Utah, USA; [4]Department of Genetics, Blavatnick Institute, Harvard Medical School, Boston, USA; [5]Howard Hughes Medical Institute, Houston, USA; [6]Dept. of Physiology, Yong Loo Lin School of Medicine, National University of Singapore; [7]Integrative Sciences and Engineering Programme, National University of Singapore, Singapore

The ability of neural stem cells (NSC) to switch between quiescent and proliferative states is fundamental for adult neurogenesis and regeneration. Microproteins or short open reading frames (sORF)-encoded peptides (SEPs), are highly abundant yet largely understudied, and their role in brain development remains unclear. Here, we demonstrate that two evolutionarily-conserved microprotein paralogs, Simba1 and Simba2, respectively, govern the reactivation of *Drosophila* quiescent NSCs. Both Simba1 and Simba2 function in NSCs and Blood-Brain-Barrier (BBB) glial cells to promote NSC reactivation. Mechanistically, Simba1 and Simba2 act as transcription factors activating the WNT/Wingless signalling pathway during NSC reactivation. We uncovered a critical role of Wg signalling molecules in promoting NSC reactivation and the translocation of Wingless from BBB glia to NSCs. Our findings reveal a novel role for microproteins Simba1/2 in regulating NSC reactivation through Wg signalling. Moreover, our bioinformatic analysis and luciferase assay suggested that the human ortholog of Simba1/2 is required for WNT signaling activation in human cells. This new regulatory paradigm may be applicable to broader cellular processes and disease conditions.



Poster Abstracts

P29

Comparative analysis of iPSC sources for NK differentiation using a proprietary accelerated protocol

Shin Yi TANG and Yuin-Han LOH

*IMCB, A*STAR, Singapore*

Induced pluripotent stem cells (iPSCs) are a promising source for generating natural killer (NK) cells for immunotherapy. In this study, we compared NK differentiation potential from iPSCs derived from $CD34^+$ hematopoietic progenitors, peripheral blood mononuclear cells (PBMCs), and fibroblasts using our proprietary express differentiation and monitoring systems. Differentiation followed a conserved trajectory marked by downregulation of CD34 and sequential upregulation of CD43, CD7, and CD56, indicating progressive NK lineage commitment. $CD34^+$-derived iPSCs demonstrated the most efficient kinetics, highest expansion potential, and superior cytotoxic activity of resulting $CD56^+CD3^-$ NK cells, whereas fibroblast-derived iPSCs showed the lowest efficiency. Our express protocol significantly reduced the differentiation timeline to 25–28 days and was validated across multiple iPSC clones from diverse origins. These findings underscore the critical impact of iPSC source on NK cell development and highlight the advantages of our proprietary system for scalable, rapid NK cell generation for therapeutic applications.

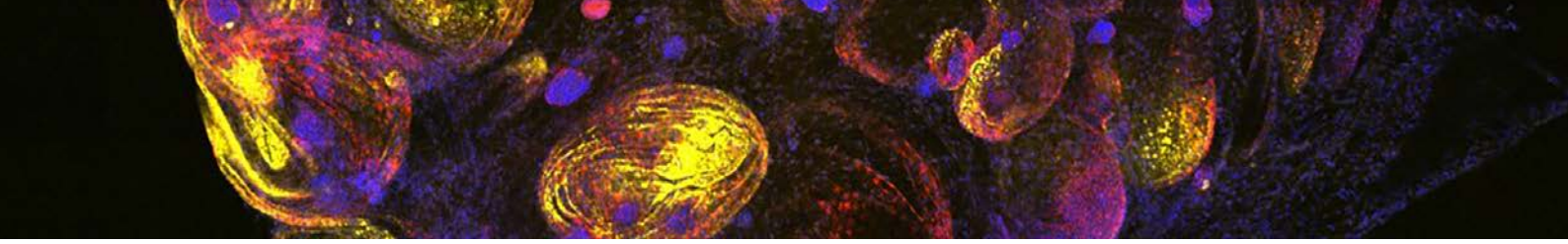
P30

The kinetochore complex proteins regulate reactivation and regeneration of *Drosophila* quiescent neural stem cells

Mahekta R Gujar[1], Yamin Htet Aumin[1], Yang Gao[1], Jiaen Lin[1], Yusuke Toyama[2, 3], Hongyan Wang[1, 4, 5]

[1]Neuroscience and Behavioral Disorders Programme, Duke-NUS Medical School, Singapore; [2]Mechanobiology Institute, Singapore; [3]Department of Biological Sciences, National University of Singapore, Singapore; [4]Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [5]Integrative Sciences and Engineering Programme, National University of Singapore, Singapore

The ability of stem cells to switch between quiescent and proliferative states is crucial for maintaining tissue homeostasis and regeneration. In *Drosophila*, quiescent neural stem cells (qNSCs) extend a primary protrusion, which is a hallmark of qNSCs. Previously, we have shown that qNSC protrusions can be regenerated upon injury. This regeneration relies on the Golgi apparatus which acts as the major acentrosomal microtubule-organizing centre in qNSCs. The Golgi-resident GTPase Arf1 and its guanine-nucleotide exchange factor Sec71 promote NSC reactivation and regeneration via the regulation of microtubule growth. The kinetochore is a conserved complex of proteins, that resides at the centromere and is essential for chromosome segregation in dividing cells. Though variants in kinetochore genes have been shown to be associated with microcephaly, very little is known about the mechanism and function of these proteins outside of the centromere in neurodevelopment. Here, we show that the kinetochore complex proteins promote acentrosomal microtubule growth and quiescent NSC reactivation. Moreover, they function upstream of Arf1 and its effector Msps/XMAP215 to regulate acentrosomal microtubule growth and quiescent NSC reactivation. Kinetochore proteins are also required for the regeneration of qNSC protrusion. In summary, our findings have identified a novel function of these kinetochore proteins in the regulation of Golgi-dependent microtubule growth, qNSC reactivation and regeneration.



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Mitochondria transplantation in Age-related Macular Degeneration: How cell source impacts outcomes

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Mitochondria dysfunction in retinal pigment epithelium (RPE) is a key driver of Age-related Macular Degeneration (AMD). Mitochondrial transplantation (MT)—the transfer of healthy, isolated mitochondria into diseased RPE—is a potential therapeutic approach. Mitochondria from different cell sources vary in structure and function. Therefore, cell source can have significant impact on MT outcomes. We hypothesize that mitochondria derived from healthy RPE are the optimal source for AMD RPE MT outcomes. In this study, we demonstrated that mitochondria isolated from stem cells (SC-mito) and RPE (RPE-mito), kept in mitochondrial isolation buffer (MIB), are pure, intact, and functional using six readouts. Interestingly, RPE showed a significant preference for SC-mito uptake under both non-stressed and oxidized low-density lipoprotein (oxLDL)-stressed conditions ($P < 0.05$). SC-mito also demonstrated superior rescue of mitochondrial membrane potential in oxLDL-treated RPEs. To translate this technology, we have done preliminary studies showing that MIB prevents mitochondria clumping and is a biocompatible injection buffer for intravitreal delivery MT up to 96 hours. In conclusion, our results suggest that SC-mito may be more suitable for MT in AMD which may be attributed to mitochondria plasticity. Future studies will be focussed on delineating this surprising phenomenon, potentially uncovering novel mitochondrial biology.

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Reconstructing sex contexts in human organoid models to study kidney and liver disorders

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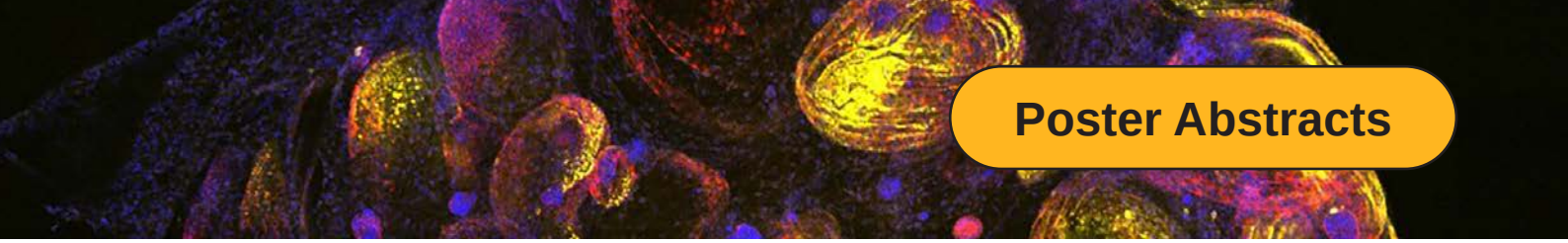
Sex differences in human disease are evident across epidemiology, pathophysiology, clinical presentation, progression, and treatment response. While sociocultural influences are widely acknowledged, the biological contributions of sex remain underexplored in clinical practice, in part due to the lack of robust experimental models that capture sex-specific contexts. These contexts are largely defined by genetic sex (sex chromosomes) and circulating sex hormones (e.g., testosterone, estrogens). We hypothesized that xenotransplantation of human organoids into immunocompromised mice could recapitulate these contexts by combining the organoid's intrinsic genetic sex with the host's hormonal environment, thereby enabling the study of sex-specific disease phenotypes. As proof of concept, we applied this organoid xenotransplantation model to polycystic kidney disease (PKD) and polycystic liver disease (PLD), two disorders with pronounced sex-dependent differences in progression and severity. The results showed that testosterone significantly promoted cystogenesis in PKD, whereas estrogen promoted cystogenesis in PLD. Furthermore, we evaluated the therapeutic potential of targeting sex hormone signaling pathways for the treatment of PKD and PLD.



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Exogenous mitochondria transfer supports long-term metabolic recovery in MELAS endothelial cells

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Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) arise from the m.3243A>G mutation in mitochondrial tRNA^Leu(UUR), leading to defective oxidative phosphorylation and progressive multi-organ dysfunction. With no curative therapy, *mitotherapy*—the supplementation of healthy mitochondria—has emerged as a potential intervention. Here, we assessed the therapeutic impact of healthy isogenic iPSC-derived mitochondria on MELAS endothelial cells. Isolated mitochondria exhibited intact cristae and high polarization (>80%) by TEM and TMRE analyses. Upon co-culture, MELAS ECs incorporated donor mitochondria in a dose-dependent manner, resulting in rapid metabolic recovery, improved tube formation, and reduced ROS. Remarkably, these benefits persisted for two weeks, with exogenous mitochondrial DNA remaining detectable in recipient cells up to four weeks post-treatment. Transcriptomic profiling revealed that only healthy mitochondria restored metabolic and ribosomal biogenesis pathways, while dysfunctional or fragmented mitochondria produced partial or transient effects. Selective retention of exogenous mitochondria occurred only when they provided a metabolic advantage, underscoring key translational potential. Together, these results underscore mitotherapy's potential beyond genetic mitochondrial disorders—to address broader metabolic and aging-related dysfunctions.

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