



8:15 a.m.	Registration	
8:55 a.m.	<b>Welcome &amp; Opening Address</b>	<b>Prof. Jonathan Loh</b> , Institute of Molecular and Cell Biology (IMCB) A*STAR & President of Stem Cell Society Singapore (SCSS)
9:05 a.m.	<b>Neural</b> Benchmarking Human Midbrain Cultures Against In Vivo Atlas From Development to Disease: Insights from Cerebral Organoid Models Refining Human Brain Organoid Models to Capture Human-Specific Features From Models to Medicines for a Rare Brain Disorder: Human Neuron and Organoid Insights into Angelman Syndrome and First-in-Class Small Molecules Organoid Culture Promotes the Expansion of Residual Pluripotent Cells and Serves as a Preclinical Assessment Tool for Tumorigenicity in Cell Therapy Products	<b>Chair: Prof. Jonathan Loh</b> , IMCB A*STAR & President of SCSS <b>Dr. Alfred Sun</b> , DUKE-NUS  <b>Dr. John Chua</b> , NUS  <b>Prof. Wang Hongyan</b> , DUKE-NUS  <b>Dr. Shawn Je</b> , DUKE-NUS  <b>Dr. Ng Shi Yan</b> , IMCB A*STAR
10:45 a.m.	Short Break	
11:00 a.m.	<b>Advanced and Pre-Clinical Models</b> Industrial Case Study: Developing a Human iPSC-Derived Complex Culture Model for Alzheimer's Disease PALO: A Physiologically Authentic Lymphoid Organoid that Recapitulates Human Immunity in a Dish Modeling Immune Development, Aging, and Diseases Using Thymus Organoids Title: To Be Confirmed	<b>Chair: Dr. Alfred Sun</b> , DUKE-NUS <b>Dr. Yeo Shi Yun</b> , MSD  <b>Dr. Andy Tay</b> , NUS  <b>Prof. Jonathan Loh</b> , IMCB A*STAR & President of SCSS <b>Dr. Andrew Gaffney</b> , STEMCELL Technologies
12:20 p.m.	Lunch & Networking	
1:15 p.m.	<b>Panel Discussion</b> Global Push to Replace Animal Testing Models	<b>Moderator: Dr. Adrian Teo</b> , IMCB A*STAR <b>Panelists: Dr. Andy Tay</b> , NUS • <b>Dr. Yeo Shi Yun</b> , MSD • <b>Dr. Andrew Gaffney</b> , STEMCELL Technologies
1:45 p.m.	<b>Precision Medicine</b> Functional Precision Oncology: From Living Tumors to Decision-Ready Therapies Introducing Project DIVERSITY – Asian Pan-Cancer Organoid Catalogue Eyes on the Future: Advancements and Challenges in Modelling Inherited Retinal Diseases with Retinal Organoids	<b>Chair: Dr. Tan Ban Xiong</b> , NUS <b>Dr. Toh Tan Boon</b> , N.1, NUS  <b>Dr. Jason Chan</b> , National Cancer Centre Singapore (NCCS), Cancer Discovery Hub (CDH) <b>Dr. Su Xinyi</b> , IMCB A*STAR
2:45 p.m.	Tea Break	
3:00 p.m.	<b>Panel Discussion</b> Clinical Applications of Organoids	<b>Moderator: Dr. Tan Ban Xiong</b> , NUS <b>Panelists: Dr. Su Xinyi</b> , IMCB A*STAR • <b>Dr. Jason Chan</b> , NCCS, CDH • <b>Dr. Adrian Teo</b> , IMCB A*STAR
3:30 p.m.	<b>Cancer Organoids</b> Patient-Derived Organoid (PDO) Models for EGFR-Mutated NSCLC Research Organoids as Discovery Models for Novel Targets in Cancer Therapy	<b>Chair: Dr. Toh Tan Boon</b> , N.1, NUS <b>Dr. Noor Rashidha Binte Meera Sahib</b> , NCCS  <b>Dr. Wu Wei</b> , SigN A*STAR
4:30 p.m.	End of event	

## Opening address



**Prof. Jonathan Loh**

Institute of Molecular and Cell Biology (IMCB) A\*STAR & President of Stem Cell Society Singapore (SCSS)

## Neural



**Chair: Prof. Jonathan Loh**

IMCB A\*STAR & President of SCSS

## Benchmarking Human Midbrain Cultures Against In Vivo Atlas



**Dr. Alfred Sun**

DUKE-NUS

Dr. Sun is an Assistant Professor at Duke-NUS Medical School, specializing in the use of human stem cells to study neurodegenerative disorders. He is a pioneer in the field of brain organoids, having co-developed one of the world's first human midbrain organoids to better model Parkinson's disease and other movement disorders. His research focuses on creating high-fidelity, lab-grown "mini-brains" that reflect human-specific genetics, aiming to bridge the gap between laboratory discovery and clinical treatments for patients in Asia and beyond.

Protocols for deriving midbrain dopaminergic (mDA) neurons for Parkinson's disease (PD) modeling and therapy remain incompletely benchmarked against in vivo references. To establish transcriptomic standards, we generated an integrated human fetal whole-brain atlas and a midbrain subatlas. Whole-brain analysis revealed strong region-specific signatures, underscoring the need for global mapping before refined midbrain annotation. We implemented this two-tier strategy, BrainSTEM (Brain Single-cell Two tier Mapping), to systematically reassess published single-cell datasets of human midbrain culture models. BrainSTEM confirmed the presence of bona fide midbrain cell types ("on-target"), but also revealed substantial populations aligning with nonmidbrain regions ("off-target"), inflating reported mDA yields across protocols. This unbiased framework enables rigorous evaluation of differentiation outcomes, clarifies current limitations of midbrain-directed models, and provides a foundation for refining protocols toward more faithful in vitro systems for PD research and regenerative applications.

## From Development to Disease: Insights from Cerebral Organoid Models



**Dr. John Chua**

NUS

Dr. Chua is an Assistant Professor in the Department of Physiology, Yong Loo Lin School of Medicine at the National University of Singapore (NUS). He is also a Principal Investigator in the Life Science Institute Neurobiology Programme and Healthy Longevity Translational Research Programme, NUS, and Adjunct Principal Investigator at the Institute for Molecular and Cell Biology. He received his BSc (Hons 2nd Upper) and MSc from the National University of Singapore, and PhD from the University of Hamburg (University Medical Center Hamburg-Eppendorf). After completing his postdoctoral training with Prof Reinhard Jahn, he became a Research Group Leader at the Max Planck Institute for Biophysical Chemistry. John's research focuses on mechanisms involved in neural circuit formation and dysfunction. His group combines cellular, biochemical, -omics and imaging methods approaches to uncover genes and regulatory pathways involved in these processes. The lab employs human PSC-derived neurons, brain organoids, and gene-editing technologies to model human neurodevelopmental disorders. He is a member of the Synaptic Gene Ontologies and annotations (SynGO) consortium, a collaboration between leading international experts on the synapse that has helped to generate a worldwide acceptable format for synapse ontology and annotation. He was awarded the NUS Research Excellence Award.

Human brain development is a prolonged and highly complex process, and disruptions during this critical period can lead to significant cognitive and behavioural impairments. Despite extensive research, the mechanistic links between these perturbations and their outcomes remain incompletely understood. Neural and cerebral organoids, which recapitulate essential features of human brain development, provide a powerful platform for modelling these processes and elucidating underlying biological pathways. In this presentation, I will highlight findings from two recent studies demonstrating how organoid-based approaches advance our understanding of neurodevelopmental disorders and neurovirulence, particularly in the context of genetic mutations and viral infections.

## Refining Human Brain Organoid Models to Capture Human-Specific Features



**Prof. Wang Hongyan**  
DUKE-NUS

Professor 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.

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. Our 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.

## From Models to Medicines for a Rare Brain Disorder: Human Neuron and Organoid Insights into Angelman Syndrome and First-in-Class Small Molecules



**Dr. Shawn Je**  
DUKE-NUS

Dr. Je is a tenured Associate Professor in the Neuroscience and Behavioral Disorders Program at Duke-NUS Medical School in Singapore. He serves as the Director of the SingHealth Advanced Imaging Centre. He received his B.S. from KAIST, his M.S. from the University of Michigan, Ann Arbor, and his Ph.D. through the National Institutes of Health (NIH) Graduate Partnership Program at the George Washington University Medical School, where he conducted research in the laboratory of Dr. Bai Lu. He completed a Howard Hughes Medical Institute (HHMI)/Duke University Medical School postdoctoral fellowship with Dr. Michael Ehlers. Dr. Je joined Duke-NUS Medical School as an assistant professor in late 2010 and was granted tenure in 2017. In 2022, he received the Scientist of the Year Award from the Ministry of Science and ICT of South Korea. Government agencies and private foundations in Singapore and Australia support his research. Dr. Je's research focuses on understanding how genes and environmental factors shape neural wiring, which is critical for developing better ways to prevent and treat brain disorders. His group has achieved high efficiency in deriving major types of cortical neurons (excitatory glutamatergic neurons and forebrain GABAergic interneurons) from human pluripotent stem cells (hPSCs). In addition, they have created the first 3D midbrain organoids that mimic sub-regions of the human brain. Dr. Je's expertise spans multiple fields, including in vitro electrophysiology, tissue engineering, cell biology, biochemistry, genetics, multiphoton imaging, and stem cell biology, which he uses to advance research on human brain disorders.

Disruptions to the *UBE3A* gene, which encodes the ubiquitin protein ligase E3A, cause Angelman syndrome (AS). However, the human mechanisms driving network hyperactivity and epilepsy remain unclear. Using human-induced neurons and brain organoids, we demonstrate that *UBE3A* restrains hyperexcitability by promoting the degradation of calcium- and voltage-dependent big potassium (BK) channels via a ubiquitin-mediated process. Increased BK channel activity increases intrinsic excitability in individual neurons and spreads as abnormal network synchronisation. Pharmacological BK antagonists normalised neuronal excitability and reduced seizure susceptibility in an AS mouse model. Based on these mechanistic insights, we identified a brain-specific BK channel complex and developed ligands that selectively engage with this complex. These first-in-class small molecules achieve brain-restricted BK targeting, restoring excitability without inhibiting BK channels peripherally. Our findings identify a BK channelopathy as a driver of epilepsy in AS and validate the use of human stem cell-derived neuronal systems for modelling developmental disease. Furthermore, they establish a translational path from cellular mechanisms to therapeutics.

## Organoid Culture Promotes the Expansion of Residual Pluripotent Cells and Serves as a Preclinical Assessment Tool for Tumorigenicity in Cell Therapy Products



**Dr. Ng Shi Yan**  
IMCB A\*STAR

Dr. Ng is Group Leader and Director of Research at A\*STAR Genome Institute of Singapore, as well as Senior Principal Investigator at A\*STAR Institute of Molecular and Cell Biology. Her laboratory pioneers the use of complex, multi-lineage neural organoids integrated with multi-omics technologies to investigate disease-relevant processes. Dr. Ng's research aims to uncover novel applications of neural organoids, as well as to use these models to identify potential targets for treating neurodegenerative diseases.

Induced pluripotent stem cell (iPSC)-derived products hold great promise for regenerative medicine, yet residual undifferentiated pluripotent cells within cell therapy products pose a significant risk of tumorigenicity. In this study, neural progenitors differentiated from human iPSCs were encapsulated in Matrigel droplets and maintained as organoid cultures for up to 120 days. Single cell RNA-seq of these organoids revealed the emergence and expansion of cell populations expressing pluripotency-associated markers. In summary, our results support the idea that long-term three-dimensional organoid culture can promote the self-renewal and expansion of residual pluripotent cells, offering an in vitro system to assess tumorigenic potential in iPSC-derived cell therapy products.

## Advanced and Pre-Clinical Models



**Chair: Dr. Alfred Sun**  
DUKE-NUS

### Industrial Case Study: Developing a Human iPSC-Derived Complex Culture Model for Alzheimer's Disease



**Dr. Yeo Shi Yun**  
MSD

Dr. Yeo is a Principal Scientist in Research Science at MSD's Translational Medicine Research Centre (TMRC), Singapore. With over 10 years in pharmaceutical R&D and capability building, she currently leads a team to drive functional validation of new drug targets and the development of translationally relevant in vitro models to advance drug discovery. Dr. Yeo holds a PhD in Integrated Biology and Medicine from Duke-NUS Graduate Medical School and has received multiple industrial awards for outstanding performance and innovation.

Alzheimer's disease (AD) remains one of the most challenging neurodegenerative disorders to model effectively due to its complex, multifactorial pathophysiology. Traditional preclinical animal models, while valuable, fail to fully capture human-specific disease mechanisms, limiting translational success. In this industrial case study, we present the development of a human induced pluripotent stem cell (iPSC)-derived complex culture model designed to better mimic the cellular and molecular features of AD. Our approach integrates multiple neural cell types, including neurons, astrocytes, and microglia, within a physiologically relevant environment to recapitulate key aspects of amyloid and tau pathology, neuroinflammation, and synaptic dysfunction. We discuss the technical considerations, validation strategies, and challenges encountered during model optimization, as well as its potential applications in drug discovery and biomarker development. This work underscores the promise of human iPSC-based platforms as next-generation tools for improving disease understanding and enhancing clinical predictivity in AD research.

## PALO: A Physiologically Authentic Lymphoid Organoid that Recapitulates Human Immunity in a Dish



**Dr. Andy Tay**  
NUS

Dr. 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. Dr. Tay 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. He is a recipient of international awards including the Terasaki Young Innovator Award and Micro and Nano Engineering Young Investigator Award. He 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.

Infectious diseases are a global-scale threat that adversely impacts human health and economy. Preclinical 2D in vitro human cell co-culture, 3D explants, human lymphoid tissues and animal models suffer from poor cell diversity, lack of 3D microenvironment, poor compatibility for long-term culture and species differences. Organoid technology is a promising alternative to existing models for immunological studies because of its physiological resemblance to human organs. Here, we describe a physiologically authentic lymphoid organoid (PALO) model with rich cell diversity, tissue organisation and biofunctions by co-culturing tonsil-derived heterologous lymphoid cells with their donor-matched stromal fibroblastic reticular cells (FRCs) through a hanging drop method. Through CyTOF, we found that two-week-old PALO contained at least 22 different immune cell types which were comparable to the cellular composition of freshly digested tonsil tissues. PALO derived from SARS-CoV-2 vaccinated donors mounted differential adaptive immune response to receptor binding domain (RBD) peptide, spike protein, inactivated virus and LNP stimulation, with increasing antibody production and immune recall response across the four stimulants, as expected. Using naïve ovalbumin and SARS-CoV-1 antigen, we found that follicular dendritic cells in PALO were able to uptake, process and present naïve antigens to B and T cells, resulting in the formation of antigen-specific antibody and T cells against the naïve antigens. The data demonstrates the promise of PALO for preclinical study of human innate and adaptive immunity against infectious diseases. In conclusion, PALO faithfully recapitulates human immunity in a dish and can be used for applications spanning infectious diseases, human inflammation and cancer immunotherapy.

## Modeling Immune Development, Aging, and Diseases Using Thymus Organoids



**Prof. Jonathan Loh**  
IMCB A\*STAR & President of SCSS

Professor 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. Prof. Loh 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 24,550 times (Google Scholar) by peers worldwide. Prof. Loh'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 (SCSS), International Committee of the ISSCR and as an executive council member of the Singapore Association for the Advancement of Science (SAAS). Additionally, he founded two biotech start-ups, InnoCellular and Genovn, and is a board member of Nasdaq-listed Cytomed Therapeutics (GDTC).

As the primary site of T cell development, the thymus is vital for preventing autoimmunity and producing effective thymocytes against pathogens and cancers. However, thymic involution and degeneration can begin as early as age one, leading to disorganized tissue and diminished immune function. Thymectomy during open- heart surgery often results in reduced peripheral lymphocytes and increased mortality, highlighting the importance of thymus preservation. To better understand these processes, we employ advanced single-cell spatial technologies to investigate thymic development, aging, autoimmunity, and thymic cancers across human life stages. This approach aims to deepen our understanding of thymic biology and uncover novel cell types and aging-related pathways. Additionally, to model thymic involution and identify regeneration strategies, we have developed a thymus organoid from pluripotent stem cells (PSCs). Using an established differentiation protocol, PSCs are assembled into embryoid bodies and differentiated at an air-liquid interface on transwells. Since the published protocol is not fully optimized, we conducted drug screenings to enhance organoid development and validated functionality by introducing human embryonic stem cell (hESC-derived hematopoietic progenitor cells (HPSCs) to assess T cell education and lineage output.

### Title: To Be Confirmed



**Dr. Andrew Gaffney**  
STEMCELL Technologies

## Panel Discussion – Global Push to Replace Animal Testing Models



**Moderator: Dr. Adrian Teo**  
IMCB A\*STAR

### Panelists:

- **Dr. Andy Tay**, NUS
- **Dr. Yeo Shi Yun**, MSD
- **Dr. Andrew Gaffney**, STEMCELL Technologies

## Precision Medicine



**Chair: Dr. Tan Ban Xiong**  
NUS

### Functional Precision Oncology: From Living Tumors to Decision-Ready Therapies



**Dr. Toh Tan Boon**  
N.1, NUS

Dr. Toh is a Senior Research Fellow and Principal Investigator at the N.1 Institute for Health (N.1) and the Institute for Digital Medicine (WisDM), National University of Singapore. He leads the Translational Core Tx Laboratory, where his research focuses on building patient-derived cancer models, including organoids, tumorspheres, and xenografts, to enable Functional Precision Oncology. His work integrates experimental assay development, genomics analyses, and data-driven drug sensitivity platforms to uncover therapeutic vulnerabilities in therapy-resistant cancers. Dr. Toh works closely with clinicians and computational scientists to translate mechanistic insights into clinically actionable strategies.

Despite major advances in genomics-guided oncology, many cancers, particularly therapy-resistant and rare malignancies, continue to lack effective and durable treatment options. Patient-derived organoids and related ex vivo tumor models offer a powerful opportunity to functionally interrogate drug response while preserving intra-tumoral heterogeneity and clinically relevant phenotypes. In this talk, I will discuss our work in establishing and the use of patient-derived models - including 2D patient-derived cells, 3D tumorspheres, and organoids - obtained directly from consented biopsies and surgical specimens to support clinically relevant applications. These "living tumor" systems form the backbone of our Functional Precision Oncology (FPO) pipeline, where rigorous assay development is integrated with genomic profiling and data-driven drug sensitivity platforms. I will highlight how these platforms enable the systematic identification and prioritisation of actionable drug combinations, particularly in therapy-refractory cancers, and how functional readouts complement molecular profiling to generate decision-ready therapeutic hypotheses. Finally, I will discuss the translational challenges and opportunities of FPO, including clinical alignment, scalability, and closing the loop from patient to model and back to patient care.

### Introducing Project DIVERSITY – Asian Pan-Cancer Organoid Catalogue



**Dr. Jason Chan**  
National Cancer Centre Singapore (NCCS); Cancer Discovery Hub (CDH)

Dr. Jason Chan obtained his medical degree from the National University of Singapore and achieved his postgraduate accreditation from the Royal College of Physicians (UK). He completed specialist training at the National Cancer Centre Singapore and subsequently obtained a Doctorate from the Cancer Science Institute of Singapore. Currently, he is Senior Consultant Medical Oncologist at the National Cancer Centre Singapore and Assistant Professor at Duke-NUS Medical School. He concurrently serves as Director of the Cancer Discovery Hub and Director of Medical Oncology Research at the National Cancer Centre Singapore. At the national level, he serves as Platform Lead for the Singapore Translational Cancer Consortium. Dr. Chan has special interests in lymphomas and rare cancers including sarcomas and melanomas. His key research interests lie in unravelling the molecular pathobiology of cancers with the aim of improving clinical care of patients inflicted with these diseases.

Patient-derived organoids (PDOs) have emerged as effective ex vivo models to study cancer biology and develop therapeutic strategies. Various studies have shown that PDOs mimic patient responses to chemotherapies. PDOs are also used for studying tumour heterogeneity by analyzing gene expression profiles, proteomics and mutational signatures and may have the potential to help facilitate clinical decision making. Recent studies show that organoids can be generated from various human cancers including liver, breast, head and neck, pancreas, colon, bladder and prostate cancers and these models are helping us to expand our knowledge on the etiology and characteristics of these malignancies. Culturing organoids can be technically challenging, but once established it can provide greater insights into translational research. The Differential In-Vitro Evaluation of Resistance and Sensitivity ("DIVERSITY") initiative is a national effort to synergize research groups in Singapore with expertise in PDO model development. STCC aims to bring together key opinion leaders (KOLs) in organoid research under a single platform to facilitate research collaborations. In this study as part of the DIVERSITY initiative, STCC will be collating the tumour organoid models available with these organoid research groups and annotate them with molecular and de-identified clinical data. The curated collection of annotated organoid models will be used to set up the DIVERSITY virtual catalogue to facilitate collaborations.

# Eyes on the Future: Advancements and Challenges in Modelling Inherited Retinal Diseases with Retinal Organoids



**Dr. Su Xinyi**  
IMCB A\*STAR

Dr. Su Xinyi is the Executive Director of the Institute of Molecular and Cell Biology (IMCB, A\*STAR) and a leading clinician-scientist advancing regenerative and precision therapies for inherited and age-related retinal diseases. Trained at the University of Cambridge (MBCChir, PhD), she integrates clinical expertise as a Senior Consultant at the National University Hospital (NUH) with translational research at IMCB. Her team develops stem cell-derived retinal models, including patient-specific retinal organoids, to uncover disease mechanisms and accelerate gene, RNA, and cell-based therapeutic development for diverse IRD genotypes. Dr. Su also serves as Co-Director of the Centre for Innovation and Precision Eye Health (NUS) and is a tenured faculty member at the Yong Loo Lin School of Medicine. She has published in leading journals including Nature Biomedical Engineering, Nature Communications, and PNAS, secured over SGD 38M in competitive grants, and received multiple international awards. She is a member of the Macula Society and co-founder of Vitreogel Innovations.

Inherited retinal diseases (IRDs) are genetically diverse disorders that cause progressive photoreceptor degeneration and vision loss. Although numerous gene and RNA therapies are emerging, their development is hindered by a critical gap: the lack of pre-clinical models that reliably replicate human retinal biology or patient-specific disease mechanisms. Retinal organoids directly address this gap by providing a human, 3D-system that mirrors retinal development, through the formation of laminated neuroepithelia with rods, cones, and supporting cells. Using optimized protocols in our laboratory, patient-derived iPSC organoids recapitulate IRD-specific phenotypes—including photoreceptor atrophy in ABCA4- and EYS-associated disease. This enables mechanistic studies previously not possible in animal models. Remaining challenges in retinal organoid technology include; variable differentiation efficiency, inner-layer degeneration, and absence of RPE and vascular interfaces. In this talk we will discuss recent advances in retinal organoids such as machine-learning selection, scaffolds, microfluidics, and bioreactors are driving “Retinal Organoids 2.0,” positioning them as essential platforms for therapeutic testing and precision medicine.

## Panel Discussion – Clinical Applications of Organoids



**Moderator: Dr. Tan Ban Xiong**  
NUS

### Panelists:

- **Dr. Su Xinyi**, IMCB A\*STAR
- **Dr. Jason Chan**, NCCS, CDH
- **Dr. Adrian Teo**, IMCB A\*STAR

## Cancer Organoids



**Chair: Dr. Toh Tan Boon**  
N.1, NUS

## Patient-Derived Organoid (PDO) Models for EGFR-Mutated NSCLC Research



**Dr. Noor Rashidha Binte Meera Sahib**  
National Cancer Centre Singapore (NCCS)

Dr. Meera Sahib is a Research Fellow at the Department of Medical Oncology at National Cancer Centre Singapore (NCCS), specializing in patient-derived organoids and translational cancer biology. Her work focuses on modelling lung adenocarcinoma using organoid systems to investigate tumor evolution, lineage plasticity and therapeutic resistance. Her team is developing optimized culture strategies focused on sustaining EGFR-mutant lung cancer organoids long term and using these models to study early resistance events and evaluate targeted therapies ex vivo.

Patient-derived organoids have emerged as transformative platforms for uncovering fundamental mechanisms of human health and disease, and cancer organoids in particular are redefining how we model tumor evolution, therapeutic response and resistance. Lung cancer organoids (LCOs) are important reductionist models that enable patient-specific tumor biology to be recapitulated in vitro. Yet, despite their promise, the successful establishment of LCOs remains difficult. Normal airway epithelium frequently overgrows tumor cells, and many cultures fail to expand long term, contributing to the generally low long-term culture success rate reported across the field. These limitations have hindered the use of organoids as reliable platforms for functional precision oncology. In our work, we optimized culture conditions specifically tailored to sustain EGFR-mutant lung adenocarcinoma (LUAD) organoids derived from patient samples. By refining growth-factor composition, we selectively enriched tumor epithelial populations, preserved lineage markers such as TTF-1 and Napsin A and maintained stable EGFR mutation allele frequencies over extended passages. Even under these optimized conditions, long-term cultures consistently revealed a basal-like transcriptional shift and a progressive loss of EGFR-TKI sensitivity. This mirrors the lineage plasticity and emergent resistance phenotypes observed clinically, positioning LCOs as powerful models to study early events in therapeutic escape. Importantly, these organoids also serve as functional drug-testing platforms. Because they retain patient-specific genetic alterations and treatment sensitivities, they offer the potential to screen targeted therapies ex vivo, identify optimal drug combinations, and ultimately improve individualized treatment strategies. Together, this work demonstrates both the challenges and transformative potential of LUAD organoid systems. By overcoming barriers such as normal-cell outgrowth and phenotypic drift, and by leveraging these models to track lineage evolution and drug sensitivity, we may move closer to using patient-derived organoids as a practical, clinically informed platform for understanding resistance and guiding precision medicine in lung cancer.

## Organoids as Discovery Models for Novel Targets in Cancer Therapy



**Dr. Wu Wei**  
SigN A\*STAR

Dr. Wu received her PhD from the National University of Singapore in 2014 with dual-training in cancer biology and mass spectrometry (MS). In this period, she was supported by the President's Graduate Fellowship and was the recipient of three international Young Investigator Awards in Berlin, Yokohama and Beijing. During her postdoc in the Netherlands, she developed diverse and sensitive affinity tools to measure signaling in the tumor micro-environment (TME), and became interested in paracrine impacts mediated through secretion and cell-cell contact. In 2017, she started her group in Utrecht University with a niche in cancer antigen discovery and TME crosstalk, focusing on the extracellular factors needed for immunosurveillance and T cell function. Since 2021, Dr. Wu served as a nominated representative from central Europe in the world Human Proteome Organisation (HUPO) council, and was appointed to the international executive committee of the HUPO Human Immuno-Peptidome Project (HUPO-HIPP). In 2022, she moved back to Singapore to join A\*STAR-SigN, focusing on cancer antigen targeting and understanding tissue microenvironmental crosstalk. Currently she is the president of the Singapore Society for Mass Spectrometry (SSMS) and involved in the core committees of world HUPO2025, HUPO2026, AOMSC 2025, AOMSC 2027, as well as the Antigen Summer School series held in Singapore in 2026.

In this talk, I will focus on our ongoing efforts to identify novel therapeutic targets in CRC, PDAC and pediatric cancers. By chemical labelling of patient-derived organoids at the cell surface, we screened the cell-surface accessible protein target repertoire to engineer novel antibody and CAR-T therapies. By rational neoantigen discovery and shortlisting, we identified highly promising cross-loadable immunopeptides. A number of these have progressed further into therapeutic development. I will also highlight the value and limitations of organoid systems for such discovery work.