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UNDERSTANDING THE BRAIN

A DEEP DIVE INTO WHAT MAKES US HUMAN



STRIDES

The Research Newsletter of
Lee Kong Chian School of Medicine

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SCHOOL OF
MEDICINE

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FROM THE VDR'S DESK

Knowing the Mind by Vice-Dean Research, Professor Lim Kah Leong



Vice-Dean Research, Professor Lim Kah Leong

I am delighted to present to you the latest edition of our research magazine, STRIDES. This issue delves into the fascinating world of neuroscience and mental health, with a special focus on Understanding the Brain. I am thrilled to share with you our main feature story that explores the latest breakthroughs and advancements in this exciting field.

The first quarter of 2023 was marked by a number of exciting research events which also includes local and international collaborations on neuroscience and mental health that brought together scholars, scientists, and experts from a variety of fields. Events such as the Inaugural Cognition Awareness Day and the School's workshop with University of British Columbia on Brain Mechanisms of Dementia enabled us to exchange ideas, collaborate with peers, and explore new avenues for scientific discovery. We look forward to building on the momentum generated by these events as we continue to advance the frontiers of knowledge and innovation.

In addition to this, I am pleased to introduce a new section in our magazine, "Behind the Scene", where we get an exclusive peek into the lives of our dedicated researchers. This month, we have the privilege of hearing from Dr Parasuraman Padmanabhan, Head of Operation at the Centre for Neuroimaging Research (CONIC), as he shares his insights and experiences in using neuroimaging modalities to unlock the mysteries of the brain.

I would like to take this opportunity to express my appreciation and gratitude to our entire research community, including our dedicated admin staff, for their invaluable contributions to our school's research endeavors. It is your hard work, dedication, and passion that allows us to continue making great strides in the field of scientific research.

Finally, I would like to welcome Associate Professor Sanjay Chotirmall our new Assistant-Dean, Research who will double up as my deputy. We look forward to hearing more from him in the future and seeing the impact of his contributions to our research endeavours.

Let us continue to push the boundaries of scientific discovery, as we strive to make a meaningful difference in the lives of people around the world. Thank you, and I hope you enjoy this latest edition of STRIDES.

Happy reading!

UNDERSTANDING THE BRAIN

A DEEP DIVE INTO WHAT MAKES US HUMAN



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Lee Kong Chian School of Medicine (LKCMedicine) has an exceptional team of faculty members to tackle one of the greatest challenge in biomedical science - understanding the brain.

Focusing on the unifying research themes of neurodegenerative disorders, brain cell biology, and neural circuits, LKCMedicine is at the forefront of neuroscience research. Working collaboratively, our clinician scientists have formed robust links, with premier clinical neuroscience institutions in Singapore, placing us in a unique position to advance our understanding of the brain and its disorders for the benefit of society.

To help us understand human intelligence, Assistant Professor Hiroshi Makino has used artificial intelligence to deconstruct biological intelligence and found that the neurons in living nervous systems encode the same learning-related information as in artificial systems, suggesting a potential mechanism for how the brain composes a new behaviour.

These discoveries point the way to further research, including how various biological intelligence domains are implemented in the brain, which could lead to better algorithms and neural network architectures for machine intelligence.

LKCMedicine's Neuroscience and Mental Health faculty members have made significant breakthroughs in their research. Assistant Professor Anna Barron and her team discovered that the translocator protein is crucial for microglia immune cells to metabolize sugar and clear amyloid plaques in the brain linked to Alzheimer's disease.

Their optogenetic technology provided new methods to treat the disease. Meanwhile, Assistant Professor Christine Cheung's research focuses on personalized blood vessel models to understand and treat vascular inflammation and diseases such as vascular dementia.

Associate Professor Yasunori Saheki's laboratory uncovered how lipid transport works in cells, which is connected to neurological disorders like Parkinson's disease. They found that GRAMD1/Aster senses and transports cholesterol, crucial for normal brain function. Additionally, his team demonstrated how four proteins work together to regulate lipid transport, preventing the buildup of lipids in cells.

Lastly, Assistant Professor Tsukasa Kamigaki and his colleagues found age-dependent degradation of memory coding in the prefrontal cortex, highlighting the importance of early interventions to mitigate cognitive aging.

These breakthroughs have immense potential to positively impact society's understanding and treatment of brain-related diseases.

Furthering LKCMedicine's Neuroscience research efforts are the The Brain Bank (Singapore) (BBS), The Dementia Research Centre (Singapore) (DCRS) and The Cognitive Neuroimaging Centre (CONIC), all of them located at LKCMedicine.

UNDERSTANDING THE BRAIN

A DEEP DIVE INTO WHAT MAKES US HUMAN



The Brain Bank Singapore

BBS is a partnership among LKCMedicine, National Neuroscience Institute (NNI), Institute for Mental Health and National University of Singapore is growing its stock of post-mortem human brain tissues. BBS has engaged community and healthcare partners to receive four brain donations and reached 250 donors by the end of 2022. Its associated research laboratory uses the post-mortem brain tissue and human stem cell-derived neurons to identify novel therapeutic options for neurodegenerative diseases, with the aim of finding insights into Asian dementia.

Dementia Research Centre (Singapore)

DCRS is conducting a five-year Biomarker and Cognitive Impairment Study (BIOCIS) with local participants to focus on 'Asian dementia'. The study revealed that Asians have a low prevalence of the amyloid beta protein and APOE4 gene but a high burden of silent strokes that increase dementia risk. The DCRS team created a first-of-its-kind strategy that repurposes two classes of drugs to curb the progression of cerebral small vessel disease in participants with mild cognitive impairment.

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The Cognitive Neuroimaging Centre (CONIC)

CONIC has been an indispensable part of Singapore's neuroscience research, serving over 50 research projects and attracting over \$122 million in grant money to NTU. CONIC's technologies have contributed to Singapore's economy, and the centre has undertaken classified government projects from DSO National Laboratories and the Home Team. The centre's new academic and industrial collaborations and contracts, including with companies such as Merck Sharp & Dohme, Claritas HealthTech, Synaptic Delver and others, demonstrate its importance as a vital component of Singapore's neuroscience research.

In conclusion, the LKCMedicine has an amazing team of neuroscience centre and researchers working hard to understand how the brain works. We have made important discoveries that could help combat could help combat neurological disorders.



3RD JAMES BEST DISTINGUISHED LECTURE BY PROFESSOR DAME SALLY DAVIES

The 3rd James Best Distinguished Lecture hosted by LKCMedicine on 24 Feb 2023 recently featured an illuminating talk by Professor Dame Sally Davies, one of the world's most respected figures in health research and policy. The lecture, titled "Improving Lives Through Science," offered insights into Dame Sally's vast experience in medicine and highlighted her commitment to using science to improve public health.

Dame Davies has an impressive track record, having served as the UK Chief Medical Officer (CMO) for eight years and as the Chief Medical Adviser to the UK government from 2011 to 2019. She is currently the UK Special Envoy on Antimicrobial Resistance, a role that allows her to continue her lifelong work on the global threat of drug-resistant infections.

In addition to her work in the UK, Dame Davies is a leading figure in global health. She has served as a member of the World Health Organization Executive Board and as co-convenor of the United Nations Inter-Agency Co-ordination Group on Antimicrobial Resistance. She has also represented the UK internationally on the subject of antimicrobial resistance (AMR) at high-level meetings such as the G7 Health Ministers' Meeting and the COP26 Summit.

At the lecture, Dame Davies shared her experience in transforming health research in the UK and highlighted the critical role of clinical research in improving a nation's health. Her strategy is "Best research for best health," aimed at improving the health and wealth of the nation through research.

She also talked about obstacles and roadblocks she faced during her work, including the lack of interest in applied and policy research.

The audience was captivated by her speaking style, and she gave key insights into how health research can advance the prevention and treatment of diseases and improve care for people around the world.



LKCMEDICINE VALEDICTORY LECTURE BY PROFESSOR PHILIP INGHAM FRS



The LKCMedicine Valedictory Lecture by Professor Philip Ingham FRS was a fitting reflection on a distinguished career in developmental biology. The event on 19 April was held on-site at the LKCMedicine HQ Lecture Theatre, and was attended by about 100 faculty members, research staff and students.

The opening remarks were given by Dean Prof Joseph Sung, who expressed his fondness for Prof Ingham and how much he will be missed at LKCMedicine. Assoc Prof Ray Dunn then took the stage and shared his own developmental biology research, crediting Prof Philip Ingham as an inspiration.

The lecture by Prof Ingham was the highlight of the event. He took the audience on a journey through the past seven decades of developmental biology, discussing some of the key breakthroughs in the field, and giving a sense of the fun and excitement of doing science during those times.

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The closing remarks were given by Vice-Dean (Research) Prof Lim Kah Leong and former LKCMedicine Dean and Visiting Professor James Best. They both thanked Phil for his contributions to the development of LKCMedicine, and acknowledged him as a good friend and colleague. Overall, the event was a celebration of Prof Ingham's career, and a reminder of the incredible contributions made by developmental biology to the life sciences over the past seventy years.

DTU-NTU JOINT WORKSHOP IN FOOD SCIENCE AND BIOTECHNOLOGY



The DTU-NTU Joint Workshop in Food Science and Biotechnology held on 14 March was more than just an online event. It was a meeting of passionate minds who shared a common goal - to make the world a better place through food science and biotechnology.

The workshop by Technical University of Denmark (DTU) and Nanayang Technological University, Singapore (NTU) brought together brought together 40 participants, including esteemed experts such as Professor Peter Preiser and DTU's Professor Charlotte Jacobsen.

NTU's Professor William Chen shared updates on zero-waste food processing and efficient food systems, driven by his desire to reduce food waste and improve sustainability. DTU's Associate Professor Aberham Hailu Feyissa explored food processing through modelling, with the aim of making food production more efficient and affordable.

The presentations by LKCmedicine Professor Wang Yulan and DTU's Professor Tine Rask Licht highlighted the importance of gut microbiome and its impact on host metabolism, showing how their research could lead to improved health outcomes for people worldwide. Meanwhile, LKCmedicine Associate Professor Yusuf Ali discussed the potential of dietary intervention to mitigate insulin-producing cell lipotoxicity, with the ultimate goal of improving the lives of those with diabetes.

The workshop also featured presentations on high-quality proteins from green biorefining and precision fermentation by DTU's Professor Peter Ruhdal Jensen. DTU's Academic Officer William Nordmark presented funding possibilities for joint collaboration, providing hope that these passionate individuals can work together to make a real difference in the world.

INAUGURAL COGNITION AWARENESS DAY



The LKCMedicine Dementia Research Centre (Singapore) (DRCS) made waves with the inaugural Cognition Awareness Day 2023, held on 23 February. The event drew over 100 attendees, who are members of the public all eager to learn about the impact of blood vessel health on cognitive disorders such as mild cognitive impairment and dementia.

Expert talks, poster displays, and exhibition booths kept attendees engaged as they gained vital knowledge about the biological aspects of cognitive disorders, lifestyle-related risk factors for dementia, and practical strategies to maintain a healthy brain. The energy in the room was palpable as LKCMedicine Dean Professor Joseph Sung warmly welcomed the attendees and Guest-of-Honour NTU Acting President, Deputy President and Provost Professor Ling San delivered an inspiring speech.



The highlight of the event was the presentation by the Director of DRCS Associate Professor Nagaendran Kandiah. Preliminary findings from the Biomarker and Cognitive Impairment Study (BIOSCIS) showed that unlike in Western populations, Asian have a low prevalence of the amyloid beta protein and APOE4 gene - significant risk factors for the disease - but a high burden of silent strokes that increase dementia risk. It also suggest that cerebral small vessel disease visualised as white matter hyperintensities (WMH) - linked to higher progression to dementia - is highly prevalent in the Singapore population.

The inaugural Cognition Awareness Day 2023 was a resounding success, inspiring attendees to take action to maintain a healthy brain and raising awareness about the impact of blood vessel health on cognitive function.

OPEN LECTURES@ LKCMEDICINE



TRANSCRIPTIONAL ADAPTATION LECTURE BY PROFESSOR DIDIER STAINIER

LKCMedicine was abuzz with excitement as Professor Didier Stainier, Director of the Max-Planck Institute of Heart and Lung Research, Bad Nauheim, Germany, presented a groundbreaking lecture on Transcriptional Adaptation (TA) on 3 Feb 2023. The event, hosted by LKCMedicine Professor Philip Ingham, was a true scientific tour de force.

Prof Stainier's research has uncovered a previously unknown process whereby certain types of deleterious mutation trigger the transcriptional modulation of other genes through degradation of the mutant mRNA and factors involved in small RNA maturation and nuclear import. Using zebrafish, *C. elegans*, and human cells, he has pioneered new insights into fundamental biological processes that have the potential to revolutionize our understanding of human health and disease.

Attendees were mesmerised by Prof Stainier's infectious passion for basic science research, which highlighted the importance of curiosity-driven science in uncovering fundamental biological processes. The lecture was a testament to the power of science to transform our understanding of the world and its potential to impact human lives in meaningful ways.

LKCMEDICINE OPEN LECTURE BY ASSISTANT PROFESSOR JENNIFER AUCHTUNG

Assistant Professor Jennifer Auchtung from the University of Nebraska-Lincoln delivered an exciting seminar on "Investigating impacts of diet-microbiota interactions on community assembly and pathogen resistance" on 8 Feb 2023. Attendees were thrilled to learn about the impact of different perturbations on microbial communities and their influence on disease susceptibility.

Asst Prof Auchtung's insights shed light on how variations in nutrients and drugs affect microbial interactions, which play a vital role in maintaining biodiversity. Her research highlighted the importance of understanding these interactions to improve disease prevention and treatment.



LKCMEDICINE AND THE FIRST AFFILIATED HOSPITAL, SUN YAT-SEN UNIVERSITY SIGN MASTER RESEARCH COLLABORATION AGREEMENT



LKCMedicine and The First Affiliated Hospital, Sun Yat-sen University (FAH-SYSU) joined forces on 30 March, 2023 signing a Master Research Collaboration Agreement at a ceremony held at the School's Novena campus. The agreement will provide a framework for project collaborations, enabling faculty members from both institutions to exchange project ideas and work together on exciting new initiatives.

FAH-SYSU is one of the largest public hospitals in the Greater Bay Area of China and renowned for its quality of healthcare services, scientific research and medical education. The hospital has won an impressive 90 national and international awards for research and development over the past 10 years.

The meeting was hosted by LKCMedicine Dean and NTU Senior Vice President (Health & Life Sciences) Professor Joseph Sung, together with Vice-Dean (Research) Professor Lim Kah Leong, Vice-Dean (Faculty Affairs) Associate Professor Andrew Tan, and several other faculty members. They had a lively discussion with Executive Vice President of Sun Yat-sen University and President of FAH-SYSU Professor Xiao Haipeng lead a delegation of 10 faculty members.

During their visit, Prof Xiao and his delegation were given a tour of the School's cutting-edge Organoid Lab and state-of-the-art Medical Library. The day concluded with a delightful lunch hosted by Prof Sung, where everyone had the chance to network and discuss exciting new possibilities for collaboration.

LKCMEDICINE-UBC VIRTUAL SYMPOSIUM ON “BRAIN MECHANISMS OF DEMENTIA”



LKCMedicine and the University of British Columbia (UBC) are taking their ongoing dialogue regarding research collaborations to new heights on 9 February 2023. In a recent virtual symposium on the theme “Brain mechanisms of dementia”, Assistant Professors Tsukasa Kamigaki and Hiroshi Makino, Nanyang Assistant Professor Christine Cheung, and Associate Professor Nagaendran Kandiah, representing LKCMedicine, presented their latest research findings alongside four exceptional speakers from UBC.

The discussions sparked many exciting opportunities for collaborative research, with Dr. Lynn Raymond from UBC and LKCMedicine Vice-Dean (Research) Professor Lim Kah Leong expressing their interest to catalyze joint efforts through pilot research grants and faculty mobility support. The enthusiasm and drive of both teams have already yielded fantastic results, and we can expect even more groundbreaking research in the future.

It's an exciting time for LKCMedicine and UBC, as we work together to tackle the complex issue of brain mechanisms in dementia. With each step forward, exciting new possibilities for collaborative research are emerging, underscoring the power of teamwork and the importance of open dialogue in advancing our understanding of the world around us.



IN PARTNERSHIP WITH NATIONAL HEALTHCARE GROUP



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The 9th NHG-LKCMedicine Research Symposium was held on 10 April 2023, and the focus was on MedTech. It was a well-attended event with about 100 participants. The opening remarks were given by Associate Professor Lim Su Chi, who set the tone for the symposium. There were four speakers who shared their research on MedTech.

Associate Professor Eric Yap talked about using genomic and microfluidic technologies to diagnose microbes, while Associate Professor Hou Han Wei shared about microfluidics and organ-on-chips for checking out vascular health. Dr Chen Kok Pun talked about the CAST of Medtech and healthcare innovation in a disruptive world, while Associate Professor Tey Hong Liang talked about creating innovative Medtech solutions to improve healthcare. The event concluded with a panel discussion with all the speakers and closing remarks by LKCMedicine Vice-Dean (Research) Professor Lim Kah Leong.

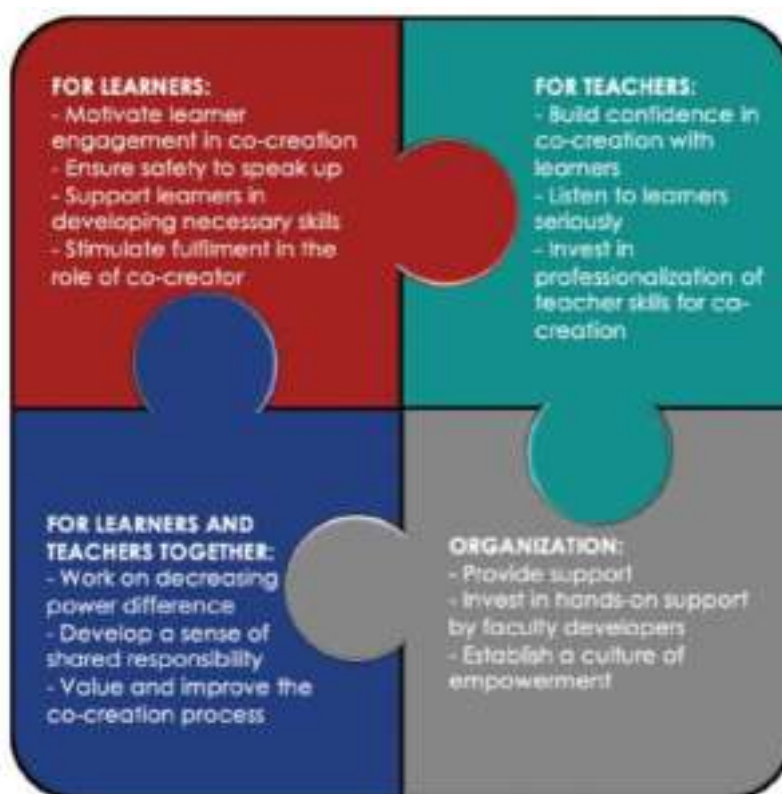
MEDICAL EDUCATION RESEARCH NEWS

EMPOWERING COLLABORATION: LKCMEDICINE'S CO-CREATION APPROACH TO MEDICAL EDUCATION

BY DR HAN SIEW PING, LECTURER, PHYSIOLOGY/MEDICAL EDUCATION

The aim of co-creation, according to LKCMedicine, is to transform medical education by fostering more collaborative and equitable partnerships among teachers, students, and other stakeholders. This approach has demonstrated its potential to improve teaching and learning experiences and to reinforce trust and relationships within the education community.

LKCMedicine has already started to put this approach into practice by promoting research collaborations among faculty, students, and Digital Learning (DL) staff. For example, a team of current M3 students and faculty, led by student Jeremy King Wang, co-authored a publication on Instagram-based horizontal learning, which was published in *Medical Education*, one of the leading journals in the field. Additionally, faculty and DL team members collaborated to produce a Twelve Tips paper on co-production in online learning, which has been accepted for publication by the highly competitive journal *Medical Teacher*.



To gain a better understanding of how co-creation works in practice, LKCMedicine investigated the working dynamics between DL staff and faculty in the co-development of online learning materials. The study revealed that, while DL staff bear growing responsibility for developing and delivering effective online learning materials, faculty retain the bulk of decision-making authority. This centralisation of agency by faculty can disempower DL and undermine the effectiveness of the production of learning materials. Consequently, LKCMedicine is advocating for a more equitable redistribution of authority and responsibility between faculty and academic support staff such as learning technologists. The findings of this study are currently under review with the journal *Advances in Health Sciences Education*.

LKCMedicine hopes that by driving co-creation initiatives, it will foster a community of teaching and learning that empowers all stakeholders to utilise their skills and knowledge fully. The goal is to drive institutional changes that promote more effective collaboration between these parties, leading to improvements in health professions education and the development of better future doctors.



LEAD EDITOR OF THE AUTHORITATIVE GUIDE "RESEARCHING MEDICAL EDUCATION"

LKCMedicine Vice-Dean (Education) Professor Jennifer Cleland is the lead editor of the book "Researching Medical Education". She co-edits this book with Prof Steven Durning by Prof Steven Durning, from the Uniformed Services University of the USA. The first edition was published in 2015 and has sold approximately 5000 paper and e-copies across the globe. Wiley recommissioned Profs Cleland and Durning to produce a 2nd edition, published in January 2023. With 30 chapters, and contributions from the "who's who" of global researchers in the field, "Researching Medical Education (Edition 2)" has been called "an extraordinary text that combines theory and practice in medical education research" and "a must-have for everyone who is curious or serious about how to do rigorous/excellent research in health professions education".

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MEDICAL EDUCATION RESEARCH PUBLICATIONS

1	Shah, A., Walker, K. A., Hawick, L., Walker, K. G., Cleland, J. Scratching beneath the surface: How organisational culture influences curricular reform. <i>Medical Education</i> . (Published online 02 December 2022) https://doi.org/10.1111/medu.14994
2	Lau, K.Y., Ang, J.Y.H. & Rajalingam, P. Very Short Answer Questions in Team-Based Learning: Limited Effect on Peer Elaboration and Memory. <i>Medical Science Educator</i> (Published online 20 December 2022). https://doi.org/10.1007/s40670-022-01716-5
3	Cleland, J., Blitz, J., Cleutjens, K. B. J. M., oude Egbrink, M. G. A., Schreurs, S., Patterson, F. Robust, defensible, and fair? The AMEE guide to selection into medical school. <i>Medical Teacher</i> (Published online 28 January 2023). https://www.tandfonline.com/remotexts.ntu.edu.sg/doi/full/10.1080/0142159X.2023.2168529
4	Cleland JA and Durning S. 2023. <i>Researching Medical Education</i> (2nd Edition). Wiley: Oxford
5	Mogali SR. Initial impressions of ChatGPT for anatomy education. <i>Anatomical Sciences Education</i> (Published online 7 February 2023) https://doi.org/10.1002/ase.2261
6	Mohamed Shah MT, Yeong LC, Cheng LT, Ang J, Yang L, Tan K, Lim CC. Future Online Radiology Education: The Importance of Curriculum. <i>Korean Journal Radiology</i> . (Published online 9 February 2023) 24(3):173-176. https://doi.org/10.3348/kjr.2023.0029
7	Ellis R, Brennan PA, Hines J, Lee AJ, Cleland J. Examining the diversity of MRCS examiners. <i>The Surgeon</i> . (Published online 25 February 2023). https://doi.org/10.1016/j.surge.2023.02.002
8	Shah, A. P., Walker, K. A., Hawick, L., Walker, K. G., Cleland, J. Context matters in curriculum reform: an analysis of change in surgical training. <i>Medical Education</i> . (Published online 3 March 2023). https://onlinelibrary.wiley.com/doi/10.1111/medu.15071

GRANT AWARDS

CONGRATULATIONS TO ALL!

A*STAR Human Health and Potential (HHP) IAF-PP

Kevin Pethe

Strategic Optimisation of mRNA vaccines for Preparedness of COVID-19 Variants

NMRC OF-IRG

Xia Yun

Preclinical evaluation of candidate PKD drugs in kidney organoid xenograft model and genetic animal model.

NMRC OF-LCG

Wang Yulan (SA)

Precision Medicine in Liver Cancer across an Asia-Pacific Network 2.0 (PLANet 2.0)

NRF-MOST Joint Grant (NRFMOSTID)

Eric Yap

Screening of SARS-CoV-2 Covalent Entry Inhibitors using Photonic Nanowell Plate with Single Virus Resolution

MOE Tier 2 Grant

Franklin Zhong

Characterizing the role of the 'ribotoxic stress-inflammasome' (RSR-I) pathway in skin antibacterial immunity

Hiroshi Makino

Compositional representations for multi-task and transfer learning

Tom Carney

Examining the altered immunological and molecular landscape of the jaw following bisphosphonate treatment to define mechanisms of bone homeostasis

MOE Tier 1 Thematic Grant

Sanjay Chotirmall

Air microbiomes and inhalable microplastics as novel pollutants in respiratory health

Lim Jue Tao

Exploring the interface of dengue, other vector-borne diseases and the environment in the Western Pacific region

MOE Tier 1 Seed Funding

Kazuyuki Kasahara

Investigating the role of gut microbiome in the cardio-protective effects of low-protein diet

Keisuke Ejima

Patient stratification for development of better isolation guideline

Industry: A*STAR Skin Research Labs

John Chambers

Consultancy work for A*STAR Skin Research Labs

RESEARCH PUBLICATIONS



ASSOCIATE PROFESSORS SANJAY CHOTIRMALL & JOHN ABISHEGANADEN

LKCMEDICINE RESEARCHERS: JAYANTH KUMAR NARAYANA, TAVLEEN KAUR JAGGI, KAI XIAN THNG

SENSITISATION TO RECOMBINANT ASPERGILLUS FUMIGATUS ALLERGENS AND CLINICAL OUTCOMES IN COPD THE EUROPEAN RESPIRATORY JOURNAL

Variable clinical outcomes are reported with fungal sensitisation in chronic obstructive pulmonary disease (COPD), and it remains unclear which fungi and what allergens associate with the poorest outcomes. The use of recombinant as opposed to crude allergens for such assessment is unknown. Aspergillus sensitisation is a treatable trait in COPD. Measuring sensitisation responses to recombinant Aspergillus allergens identifies an important patient subgroup with poor COPD outcomes that remains overlooked by assessment of only crude Aspergillus allergens.

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ASSOCIATE PROFESSOR JIMMY LEE, PROFESSORS JOSEPH SUNG AND JOHN CHAMBERS

THE SINGAPORE NATIONAL PRECISION MEDICINE STRATEGY

NATURE GENETICS

Precision medicine promises to transform healthcare for groups and individuals through early disease detection, refining diagnoses and tailoring treatments. Analysis of large-scale genomic-phenotypic databases is a critical enabler of precision medicine. Although Asia is home to 60% of the world's population, many Asian ancestries are under-represented in existing databases, leading to missed opportunities for new discoveries, particularly for diseases most relevant for these populations. The Singapore National Precision Medicine initiative is a whole-of-government 10-year initiative aiming to generate precision medicine data of up to one million individuals, integrating genomic, lifestyle, health, social and environmental data. Beyond technologies, routine adoption of precision medicine in clinical practice requires social, ethical, legal and regulatory barriers to be addressed. Identifying driver use cases in which precision medicine results in standardized changes to clinical workflows or improvements in population health, coupled with health economic analysis to demonstrate value-based healthcare, is a vital prerequisite for responsible health system adoption.

RESEARCH PUBLICATIONS



ASSOCIATE PROFESSORS JOANNE YUEN YIE NGEOW & SUNNY WONG

LKCMEDICINE RESEARCHERS: ALVIN NG

GLOBAL EPIDEMIOLOGY AND GENETICS OF HEPATOCELLULAR CARCINOMA

GASTROENTEROLOGY

Hepatocellular carcinoma (HCC) is one of the leading cancers worldwide. Classically, HCC develops in genetically susceptible individuals who are exposed to risk factors, especially in the presence of liver cirrhosis. Significant temporal and geographic variations exist for HCC and its etiologies. Over time, the burden of HCC has shifted from the low-moderate to the high sociodemographic index regions, reflecting the transition from viral to nonviral causes. Geographically, the hepatitis viruses predominate as the causes of HCC in Asia and Africa. Although there are genetic conditions that confer increased risk for HCC, these diagnoses are rarely recognized outside North America and Europe. In this review, we will evaluate the epidemiologic trends and risk factors of HCC, and discuss the genetics of HCC, including monogenic diseases, single-nucleotide polymorphisms, gut microbiome, and somatic mutations.



ASSISTANT PROFESSORS ANNA BARRON & SARAH LANGLEY

LKCMEDICINE RESEARCHERS: LAUREN H FAIRLEY, KEI ONN LAI, JIA HUI WONG, WEI JING CHONG, ANSELM SALVATORE VINCENT, GIUSEPPE D'AGOSTINO, ROSHAN R NAIK, ANUSHA JAYARAMAN

MITOCHONDRIAL CONTROL OF MICROGLIAL PHAGOCYTOSIS BY THE TRANSLOCATOR PROTEIN AND HEXOKINASE 2 IN ALZHEIMER'S DISEASE

PNAS

Microglia are responsible for protecting the brain. Defense demands the rapid production of large amounts of energy. But how microglial metabolism is controlled to fuel defense responses such as phagocytosis remains poorly understood. We demonstrate that mitochondrial translocator protein (TSPO) and hexokinase-2 play key roles in the control of microglial metabolism and phagocytosis by coordinating the balance of energy production via two major metabolic pathways. Microglia lacking TSPO resembled dysfunctional microglia observed in aging and Alzheimer's disease, and this could be partially reversed by blocking hexokinase-2 binding to the mitochondria. We find that targeting mitochondrial hexokinase-2 binding may offer an immunotherapeutic approach to inhibit glycolytic metabolic reprogramming and promote microglial phagocytosis in Alzheimer's disease.

INNOVATION AND ENTREPRENEURSHIP ACTIVITIES



EXPLORATORY TRANSLATIONAL GRANT CALL LAUNCHED IN COLLABORATION BETWEEN THE NATIONAL HEALTH INNOVATION CENTER



Innovation and creativity are vital in finding solutions to the world's most pressing problems, and healthcare is no exception. On March 22, 2023, the Office of Innovation and Enterprise (OIE) at the Lee Kong Chian School of Medicine organized an information session to introduce their latest initiative - the LKCMed-NHIC Exploratory Translational Grant Call 2023. This grant is designed to provide seed funding for early-stage innovation projects, and the session aimed to educate interested parties on the grant's requirements and application process.

This internal grant is a collaboration between LKCMedicine and the National Health Innovation Centre (NHIC) to support the development of solutions that are commercially viable and address unmet healthcare needs. The grant will not only provide funding but also offer opportunities for project teams to seek further competitive funding at the national level.

Faculty members, research staff, and members of the National Healthcare Group attended the information session to learn more about the grant and NHIC's support services. This collaborative effort between LKCMedicine's OIE and NHIC is a crucial step towards building a culture of innovation and enterprise within the school, and the impact of this grant will undoubtedly be felt in the broader healthcare industry.

INNOVATION AND ENTREPRENEURSHIP ACTIVITIES



LKCMEDICINE HOSTS THE EMBASSY OF SWEDEN & OLINK PROTEOMICS



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Innovation and collaboration are essential components in advancing the healthcare industry, and recently, the LKCMedicine's Office of Innovation and Enterprise (OIE) hosted a groundbreaking meeting with the Embassy of Sweden, Business Sweden, and Olink Proteomics. Held on Friday, 10 March 2023, this meeting discussed potential collaboration models and how Olink's platform technology could benefit the faculty and researchers at LKCMedicine.

The meeting was led by Associate Professors Kevin Pethe and Sunny Wong, along with Assistant Professor Bennett Lee, Dr Ervinna Pang, Dr Tay Puei Nam, and Ms Kiruthika. Business Sweden, a joint venture between the Swedish state and the Swedish business sector, and Olink Proteomics, a Swedish company providing products and services in the protein biomarker discovery field, were among the attendees.

During the meeting, the delegates were given a tour of the research infrastructure and facilities at the Clinical Sciences Building, and potential collaboration models were discussed. The groundbreaking possibilities for collaboration, research, and development in the field of protein biomarker discovery, opened up by this meeting, holds promise for the future of healthcare.

WOMEN IN SCIENCE @LKC MEDICINE



ROUNDTABLE WITH PROFESSOR DAME SALLY DAVIES FOR FEMALE FACULTY AND CLINICIAN-SCIENTISTS

With the kind coordination by Lee Kong Chian School of Medicine's External Affairs, LKCMedicine female faculty and clinician-scientists from National Healthcare Group had the opportunity to meet with Professor Dame Sally Davies (40th Master of Trinity College, Cambridge University, and UK Government's Special Envoy on Antimicrobial Resistance) on 20 February 2023, while she was in town to speak in the James Best Distinguished Lecture. Dame Sally shared her experience as a policy maker, how she broke the glass ceiling and persisted her faith and belief during difficult times with effective leadership and management. She encouraged female scientists to be bold, and work closely with each other to strive for new possibilities. It was a wonderful one-hour session to learn from Dame Sally regarding pathways to succeed as a female leader.

WOMEN IN SCIENCE @ LKCMEDICINE PLENARY SPEAKER SERIES: PROFESSOR DORIS YOUNG

The Women in Science @ LKCMedicine Plenary Speaker Series welcomed a distinguished speaker in adolescent medicine, Professor Doris Young, on 3 March 2023. Prof Young electrified the audience with her passionate mission to achieve Equal Opportunity for Women in the Workplace, sharing insights from her role as Associate Dean Equity and Staff Development (ESD) at the University of Melbourne.

With captivating personal and professional experiences as a senior woman in academic medicine, Prof Young highlighted the importance of positive initiatives and programmes that many universities worldwide have developed. These programmes provide mentorship support and leadership training to increase the participation and career progression of women.



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WIS@LKCMEDICINE - OIE PLENARY SPEAKER SERIES: DR ALEXANDRIA FORBES

On 18 April, Dr Alexandria Forbes, the CEO and Founder of MeiraGTx, shared her journey in the field of genetic medicine to an audience of 40 people at LKCMedicine. Hosted by Professor Philip Ingham FRS, she spoke about her Zoology degree from University of Cambridge and her research on the Hedgehog gene during her PhD at University of Oxford. She also shared her post-doctoral fellowships in the US and how it allowed her to identify genes important for germ cell migration.

Dr Forbes also talked about her experience working in a New York healthcare hedge fund, which led her to start MeiraGTx, a biotech company focused on genetic medicine. She shared that the company has fully integrated capabilities in gene therapy discovery, development, and GMP manufacturing, as well as a novel technology that regulates mRNA formation through orally administered small molecules.



WOMEN IN SCIENCE @LKC MEDICINE

VIRTUAL LUNCH & LEARN WORKSHOP WITH DR HELENA KIM-SINHA



In the fast-paced world of academia, leadership can be a complex and challenging field to navigate. On 27 March 2023, Dr Helena Kim-Sinha, a renowned coaching psychologist and best-selling author of "Soft Skills for Hard People," conducted a virtual workshop that shed light on the essential elements of successful leadership in universities and labs.

With expertise in working with elite leaders, academics, and scientists, Dr Helena presented the three fundamental elements that are vital for inspirational leadership in academia - confidence, coaching, and conflict management. Her workshop, "3 C's for Inspirational Leadership in Academia," was a stimulating dialogue that engaged the 35 participants in attendance.

From teaching key pointers such as how courage is a choice, to highlighting how confidence is acquired, Dr Helena's candid first-hand practical tips and advice on managing relationships in the workplace during the Q&A session held at the end of the workshop further enriched the participants' experience. Dr Helena's workshop was an invigorating and informative experience for all who attended, leaving them with valuable insights and a renewed sense of purpose in their roles as academic leaders.

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BREAKING NEW GROUND – WIS @ LKC MEDICINE PODCAST WITH FEMALE CLINICIAN-SCIENTISTS



In episodes 7-10, four outstanding female clinician-scientists shared about their research interests, their paths, the role of women in science, as well as tips on well-being and self-care. Check out the inspiring episodes at <https://soundcloud.com/user-953589002>

Episode 7: Assistant Professor Shruti Bhatt (Department of Pharmacy, National University of Singapore, member of the European Molecular Biology Organization (EMBO) Global Investigator Network)

Episode 8: Dr Jingmei Li (Group Leader of Laboratory of Women's Health & Genetics, Genome Institute of Singapore, Agency for Science, Research and Technology)

Episode 9: Associate Professor Carmen Wong (Department of Pathology and the State Key Laboratory of Liver Research, the University of Hong Kong)

Episode 10: Professor Reshma Taneja (Head of Department of Physiology at Yong Loo Lin School of Medicine, National University of Singapore)

LEARN HAPPENINGS



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LEARN SYMPOSIUM 2023

For many early career researchers, showcasing their work and exchanging ideas with their peers and mentors is a crucial step towards achieving their career goals. On 3 March, the LKCMedicine Early Researchers' Network (LEARN) organised its 2nd LEARN Symposium, bringing together more than 64 PhD students, research assistants, associates, and fellows from across the university to highlight their early research work, foster collaboration and exchange ideas.

The symposium was a rare opportunity for early career researchers to engage with their peers and receive valuable insights from a panel of distinguished speakers, making it an event that many had eagerly awaited. The excitement and anticipation were palpable as Vice-Dean (Research) Professor Lim Kah Leong delivered his opening remarks, setting the stage for what would be a stimulating and informative day for all.

GRADUATE STUDENTS NEWS

LKCMEDICINE GRADUATE STUDENT WINS FIRST PRIZE IN PECHAKUCHA COMPETITION



LKCMedicine graduate student Michelle Law was awarded first place in a PechaKucha competition at the 36th International Conference for Antiviral Research (ICAR) in Lyon, France held from 13 to 17 March. ICAR is the main event of the International Society for Antiviral Research, an internationally recognised organisation for scientists involved in basic, applied, and clinical aspects of antiviral research.

At the PechaKucha competition, graduate students and post docs presented their research in a way that was designed to entertain and inform their audience with 15 slides in 20 seconds each. Michelle's talk combined bagels and Michelle Yeoh's Oscar winning movie, "Everything, everywhere, all at once" into a presentation on chikungunya virus RNA capping. The well-received talk which incorporated science, storytelling and humour was awarded the first prize of €250. Michelle and fellow LKCMedicine graduate student Tan Yaw Bia each received travel grants of USD400.

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LKCMEDICINE GRADUATE STUDENT WINS HIGHEST RATED ABSTRACT AWARD AT OARSI 2023 WORLD CONGRESS ON OSTEOARTHRITIS



Dr Bryan Tan Yijia, a PhD student of Prof Josip, won the highest-rated abstract award at the OARSI 2023 World Congress on Osteoarthritis – Challenges Ahead in OA Research, held in Denver, Colorado, USA from 17 – 20 March 2023. The conference drew more than 1200 attendees from over 40 countries, with over 200 oral presentations. Dr Bryan Tan's presentation was on the Collaborative Model of Care Between Orthopaedics and Allied Healthcare Professionals (CONNECT) for Knee Osteoarthritis, showcasing a 12-month follow-up of an effectiveness-implementation hybrid trial.

COLLABORATIVE MODEL OF CARE BETWEEN ORTHOPAEDICS AND ALLIED HEALTHCARE PROFESSIONALS (CONNECT) FOR KNEE OSTEOARTHRITIS: 12-MONTHS FOLLOW-UP OF AN EFFECTIVENESS-IMPLEMENTATION HYBRID TRIAL

B. Tan¹, M. Pereira², S-Y. Yang¹, C. Lim¹, C. Tan¹, E. Woon³, Y. Pua⁴, J. Ng⁵, K. Lee⁶, A. Briggs⁷, D. Hunter⁸, S. Skou⁹, J. Thumboo¹⁰, J. Car¹¹: ¹Woodlands Hlth., Singapore, Singapore, ²Natl. Hlth.care Group, Singapore, Singapore, ³Nanyang Technological Univ., Singapore, Singapore, ⁴Singapore Gen. Hosp., Singapore, Singapore, ⁵Ministry of Hlth.Holdings, Singapore, Singapore, ⁶Tan Tock Seng Hosp., Singapore, Singapore, ⁷Curtin Univ., Perth, Australia, ⁸Univ. of Sydney, Sydney, Australia, ⁹Univ. of Southern Denmark, Denmark, Denmark

This presentation was co-authored by LKCMedicine's faculty, Prof Josip Car, and research staff, Eugene Woon. Dr Tan's achievement is an excellent representation of the quality of research conducted by LKCMedicine's team and the institution's commitment to advancing healthcare research. The award also underscores the significant contribution of LKCMedicine's research towards improving patient care and outcomes.

BEHIND THE SCENE



**WITH DR PARASURAMAN PADMANABHAN,
HEAD OF OPERATION, CENTRE FOR
NEUROIMAGING RESEARCH (CONIC)**

1) How is research being conducted at CONIC?

CONIC is one of the six strategic shared research facilities of NTU, serving the whole academic community with a platform of advanced human brain imaging, brain activity monitoring and brain stimulation instruments as well as advice and expertise in designing, performing and analysing experiments. Since its establishment in 2017, CONIC has performed more than 50 research projects with the involvement of more than 2000 research subjects. Approximately 20% of the projects are initiated in-house in CONIC and 80% of the research projects are initiated by NTU researchers or collaborative partners outside NTU. Since CONIC is one of the few NTU research facilities which require medically qualified personnel with AHPC license, all research activities are approved by IRB and follow strict protocols complying with MOE, HSA, HBRA and PDPA regulations.

After discussing and establishing the research protocols with CONIC experts, the PI of the research project should obtain an IRB permission to start the project. All the experimental subjects coming to CONIC undergo a safety briefing before the brain scanning starts. The subjects usually change their clothes and get a laboratory attire. The preparation for the imaging procedures may take up to one hour, and the imaging procedures themselves may also take often one hour, depending on the imaging modality. The most commonly used imaging equipment is the magnetic resonance imaging or MRI scanner, followed by the magnetoencephalography or MEG scanner. The other modalities include electro-encephalography or EEG, near infrared spectroscopy or NIRS, transcranial magnetic stimulation or TMS and transcranial DC stimulation or tDCS.

2) What are some difficulties that you have experienced and how you came up with a solution?

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In the past years the greatest challenge we experienced was related to COVID. We had to close down the facility for several months, and when we can restart our activities, first we could only do one scan a day and later two scans a day. We face another challenge: we are often performing seven scans a day. This is our capacity limit as each research scan may take up to 2.5 hours. The demand for scans from our researchers is higher than our daily capacity. As a result, we work on weekends regularly.



3) Who are the some of the core members of CONIC? How do they contribute to CONIC?

CONIC has a core team consisting of researchers, engineers, physicists and most importantly radiographers. The radiographers are medical professionals with AHPC license and without them no investigations in our most important medical imaging device, the MRI scanner, would be possible.

But CONIC is more than just a core team: since it is a research imaging facility working with human subjects, it has a physician with a Singaporean medical license too. It also has a Steering Committee consisting of representatives of the three Colleges of NTU (Science, Humanities, Engineering) as well as LKCMedicine and NHG. And finally, CONIC is a member of the NTU Centre for Strategic Research Facilities (CSRf) which has a coordinating role.

IN CONVERSATION



ASSOCIATE PROFESSOR NG OON TEK

Associate Professor Ng Oon Tek was a recipient of the NMRC Overseas Research Fellowship. His initial research training involved a Master of Public Health degree at Johns Hopkins Bloomberg School of Public Health followed by a year-long research attachment with a US NIH funded group led by Prof Thomas Quinn. His further research work in Singapore was carried out with support from the NMRC Transition Award and Clinician Scientist Award funding programs.

Associate Professor Ng has an interest in research integrating public health, laboratory medicine and clinical medicine to improve patient outcomes. Previously, he worked together with colleagues at TTSH and other institutions on in-house HIV tests for clinical care. These tests were successfully used for patient care at the HIV clinic in TTSH and other institutions. His current research interest focuses on antimicrobial resistance, especially carbapenem-resistant Gram-negative infections. He is a steering committee member of the Carbapenemase-producing *Enterobacteriaceae* in Singapore (CaPES) study group, which collects retrospective clinical data and samples on all known CPE-positive patients in Singapore public hospitals.

1) Can you tell us a bit about your current research projects?

One of the focal areas of my research work is on antimicrobial resistance (AMR) in Gram-negative bacilli, especially carbapenem-resistant *Enterobacteriales* (CRE), relying on the combined analysis of whole-genome sequencing (WGS) and epidemiological data. As part of the CaPES steering committee, we recently completed a study on the transmission dynamics of carbapenemase-producing *Enterobacteriales* (CPE) across public hospitals in Singapore based on a nationwide retrospective cohort over 4.7 years. A lead manuscript on this work has been published in Nature Communications (PMID: 35650193), suggesting the presence of persistent CPE reservoirs in the hospital environment and revealing that plasmid-mediated transmission accounted for 50% of CPE dissemination. Following successful publication of the initial work, our current ongoing work aims to study plasmid evolution and identify genetic determinants of plasmid persistence using a dataset of closed CPE genomes over the same study period. Another ongoing study, funded by NMRC CSA-INV, is a randomized clinical trial on oral capsule-administered faecal microbiota transplantation (FMT) for intestinal decolonization of carbapenemase-producing organisms (CPO), which aims to translate FMT as a clinical intervention for CPO decolonization to reduce CPO-intestinal carriage and hence CPO transmission, morbidity and mortality.

2) How does your partnership with LKCMedicine contribute to the advancement of your research goals?

The research projects that I oversee benefit greatly from ongoing collaborations with fellow researchers from LKCMedicine. An aspect of the plasmid evolution research work is in collaboration with Asst Prof Bernett Lee, in which the aim is to establish and benchmark a method for determining plasmid linkage.

I am also a Co-Investigator together with A/Prof Sunny Wong on a recently awarded NMRC Open Fund - Large Collaborative Grant (OF-LCG), where our research theme aims to understand gut colonization by carbapenem-resistant Gram-negative bacteria to prevent AMR transmission and infections. This will involve development of a clinically relevant human microbiota-associated mouse model of intestinal carbapenem-resistant *Enterobacteriales* carriage and decolonization, and discussions have also been initiated with the LKCMedicine Animal Research Facility for proposed plans on setting up of the mouse model. In line with the aims of the CaPES study group, it is also encouraging to contribute to research work led by other groups with similar interests, one such example being the collaborative work with Asst Prof Guan Xue Li on lipid metabolism in carbapenem-resistant *K. pneumoniae*. Overall, collaborative work with LKCMedicine colleagues is synergistic and contributes to shared research goals.

3) What are the challenges of integrating public health, laboratory medicine, and clinical medicine to improve patient outcomes, and how are you addressing them?

Effective communication across different disciplines is a key challenge in integrating public health, laboratory medicine, and clinical medicine. Ongoing communication efforts to better understand the different domains can help address this challenge.

4) Could you discuss a recent breakthrough in technology for clinical diagnostics and its potential benefits for patients?

A recent breakthrough is using whole-genome sequencing technology to investigate transmission of antimicrobial resistant organisms and genes, which can benefit patients when the information is applied to interrupting AMR transmission.

5) In your opinion, what are the most exciting areas of research in your field right now, and where do you see the most potential for growth and innovation in the years to come?

An exciting area of research is the role of horizontal gene transfer (HGT) in spreading AMR genes. Traditionally, the spread of AMR is thought to occur through bacterial reproduction and transmission, which largely applies to Gram-positive bacteria. However, Gram-negative bacteria are now recognized as a significant AMR threat, with HGT via plasmid conjugation having a large role in the spread of AMR genes. HGT is challenging to detect using conventional methods focused on clonal transmission. Therefore, further research is necessary to develop methods to fill this gap. One of our hopes is that whole-genome sequencing would become routine for understanding AMR transmission and contribute on a day-to-day basis to preventing onward transmission of AMR.

To all aspiring researchers, I urge you to pursue your passion for clinical research as it offers a sense of fulfillment by addressing real-world problems. I speak from personal experience, having received tremendous support and guidance from the seniors in the Infectious Disease department, particularly Prof Leo Yee Sin, who mentored me in my CSA applications. So go ahead and chase your dreams in research - it can be an immensely rewarding journey!

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