

MediCine

A PUBLICATION OF THE YONG LOO LIN SCHOOL OF MEDICINE

ISSUE 49 FEB 2024



WHY IS CANCER SO HARD TO TREAT?

Important advances in recent years offer hope but further research is vital

INNOVATIVE STRATEGIES TO DELIVER LOW-CARBON, HIGH-VALUE CARE

That is the mission of the newly launched
Centre for Sustainable Medicine

p.05

A YEAR IN DISASTER MEDICINE

NUS Medicine alumnus shares fellowship
experience at Harvard Medical School

p.49

Contents

Dossier

- 02** Spotlighting Discussion on the Health of Asian Women
- 05** Responding at pace to Climate Change: Developing Innovative Strategies to Deliver Low-carbon, High-value Care

In Vivo

- 08** MEGiCal Moments at NUS Medicine Educators' Day 2023

Science of Life

- 11** Groundbreaking Telesurgery Trial Spanning Over 5,000km
- 13** The Future of Medicine: Revolutionising Healthcare with Digital Solutions
- 16** Nano-sized Cell Particles Are Promising Intervention Tools in Treating Infectious Diseases
- 19** Game Changer for Future Production of Vaccines and Therapeutics to Fight Infectious Disease

Insights

- 20** Why is Cancer So Hard to Treat?

Ethically Speaking

- 25** Small Country, Large Research Trials – What Singapore Can Learn from Denmark

All in the Family

- 28** Neighbourhood Health Service 2023: Touching Lives, Serving the Underserved

Nursing

- 31** NUS Nursing Nets Fourth American Academy of Nursing Fellowship

Affairs of the Heart

- 33** Winning Hearts and Minds: Multidisciplinary Team Probes Mysteries of Cardiocerebral Diseases

A World in a Grain of Sand

- 36** The Road Less Travelled – Splicing in Trans: From a Natural Phenomenon to Gene Therapeutic Applications

The Last Mile

- 40** Part 2: What the Living Can Learn from the Dying (and Their Families)

Student Matters

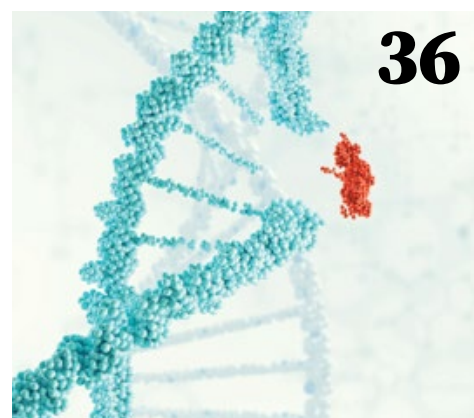
- 44** Looking for the Right Stuff – The NUS Medicine Admissions Exercise
- 47** University Scholars Leaders Symposium: Broadening Horizons and Empowering Future Health and Sustainability Champions

People of NUS Medicine

- 49** Understanding Disaster Medicine

The Banyan Tree

- 52** The Era of Extended Reality (XR) in Healthcare: Are Hospitals Prepared for the Future?
- 55** Take 5: Q&A with DTX HealthSG Leadership Masterclass 2024 Speakers



MediCine

MediCine is published quarterly by the communications office of the NUS Yong Loo Lin School of Medicine.



Yong Loo Lin
School of Medicine

NUS Yong Loo Lin
School of Medicine
1E Kent Ridge Road
NUHS Tower Block, Level 11
Singapore 119228

Email medcomms@nus.edu.sg
Web medicine.nus.edu.sg

Follow us on



@NUSMedicine



@NUS Medicine



NUS Yong Loo Lin
School of Medicine

Dean's Message

Dear Reader,

As 2024 unfolds, I would like to provide a quick review of the progress made by our School. Even as we equip our students with the knowledge, skills, and mindset to become competent and compassionate doctors and nurses, we are cognisant of the need to prepare them for the healthcare challenges of the future as the Singaporean population ages.

We launched the new Common Curriculum for Healthcare Professional Education to align with the government's 'Healthier SG' initiative. Comprising five courses and an immersive *Longitudinal Patient Experience (LPE)*, the new Common Curriculum for Healthcare Professional Education is designed to focus on preventive healthcare and facilitate ageing in place using technology and analytics.

Our research programmes are making good, steady progress. Singapore is perfectly placed to lead the understanding of Asian Health and Disease, given the ethnic makeup of our population. By delving deeper and getting a better understanding of how biology, natural history, lifestyles, and genetic susceptibility affect therapeutic responses to diseases in Singapore, such as cardiovascular-metabolic diseases, we can potentially reverse disease trajectories not just in Singapore but Asia. In my last message, I mentioned Project RESET, led by Professor Roger Foo and his team at the Cardiovascular-Metabolic Disease Translational Research

Programme. RESET is the first of many NUS Medicine projects that can be game-changers for advancing understanding of Asian patterns of diseases and health.

Second, with Singapore being one of the fastest ageing populations in the world with steadily rising life expectancy, one of the demands of the healthcare sector will be to enable healthier ageing of the population. While Singapore's life expectancy is 83 years, our healthy life expectancy is 73 years. This means that Singaporeans can expect to spend 10 years in ill health. This is why one of the ambitious research efforts here at NUS Medicine aims to increase the Healthy Life Expectancy or Healthspan of Singaporeans by five years by 2050.

Our scientists are looking into refining current diagnostics and biomarkers to better risk stratify individuals and the Healthy Longevity Translational Research Programme is focused on creating a steady flow of research into geroscience that includes preclinical translational approaches to slow or reverse effects of ageing and holding trials to test the efficacy of healthy longevity promoting interventions.

This requires our scientists to work closely with clinicians in our health system and offer us ways to understand why our patients and the population behave the way we do and what might 'nudge' them to change; what organisational support we need to improve our practices; and what incentives we ourselves



will respond best to. At NUS Medicine, we are blessed to have behavioural and social scientists, health economists and people who understand organisational behaviours with us at the Centre for Behavioural and Implementation Science Interventions, to help fast-track the translation of clinical research and evidence into practice, routine evidence-based practice in healthcare delivery, and embed these practices into our health system.

I end this quick review of our work with more encouraging news: in the Times Higher Education rankings of medical schools for 2024, NUS Medicine has risen from being ranked #3 in Asia (2023) to #2 in Asia (2024).

This year, we are tied with the Karolinska Institute of Sweden for 16th place among medical schools in the world. The Karolinska is a very distinguished university dedicated to Medicine established in 1810, before Singapore was even founded by Sir Stamford Raffles.

We are gratified and appreciative that the hard and good work of our colleagues and students has enabled the Yong Loo Lin School of Medicine to be ranked among the best medical schools in the world.

Yap Seng



Spotlighting Discussion on the Health of Asian Women

Poised to become a major global research centre that adopts a holistic and systematic approach to Asian women's health and well-being, the Global Centre for Asian Women's Health (GloW) at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), was officially launched by Ms Indranee Rajah, Minister in the Prime Minister's Office at the inaugural Singapore Women's Health conference, on 10 November 2023.

Women face distinct and various challenges throughout different stages of their lives, one of them being conception and childbirth.

Facing unparalleled risks through these stages of their lives, some outcomes include conditions such as hypertensive disorders in pregnancy, gestational diabetes mellitus, preterm birth, and more.

Hence, it is undeniable that the health of women is a

pivotal topic that needs to be studied closely, with close ties with the family and society. Investing in women's health ensures healthier and more productive individuals, happier families, and a better society in general. Yet, much remains to be done in the field of research on women's health and well-being.

A global centre dedicated to furthering the cause of women's health

Dedicated to the advancement of women's health and longevity, the inaugural conference organised by GloW was held from 9 to 11 November 2023.

Photo:
(From left to right) Professor Aaron Thean, Deputy President (Academic Affairs) and Provost, National University of Singapore (NUS), Professor Chong Yap Seng, Dean, NUS Medicine, Ms Indranee Rajah, Minister in the Prime Minister's Office and Second Minister for Finance and National Development, Professor Zhang Cuijin, Director, GloW, NUS Medicine, and Professor Michelle Williams, Former Dean, Harvard T.H. Chan School of Public Health, at the launch of GloW.

Established under the auspices of NUS Medicine, GloW is a major research centre based in Asia, focusing specifically on health issues of Asian women worldwide. Through embracing a holistic and systematic approach to health, it aims to tackle emerging public and family concerns.

It conducts cutting-edge research on the health and well-being of women and their families and aims to narrow the gaps between research, policy and practice.

“At GloW, we have the privilege to explore cutting-edge research, engage in thought-provoking discussions, and form collaborations that can shape the future of women’s health. Our ultimate mission is to improve women’s health in Asia and beyond,” said Professor Zhang Cuijin, Founding Director of GloW at NUS Medicine.

The four primary missions of GloW are:

- Addressing common and important clinical and public health problems concerning women, children, and their families.
- Identifying modifiable risk factors of common disorders related to women’s health by examining the complex interplay of factors, which range from dietary and lifestyle, to psychosocial, behavioural, environmental, genetic, and epigenetic.
- Translating scientific knowledge into clinical and public health practices that can lead to advancements in early prediction, prevention, diagnosis, and treatment of common disorders concerning women’s health and well-being across their life courses and generations.
- Training a new generation of

medical and public health professionals to become leading transdisciplinary investigators and future leaders in women’s health with a life-course approach to health education.

The centre was officially launched by Ms Indranee Rajah, Minister in the Prime Minister’s Office and Second Minister for Finance and National Development at its inaugural three-day Singapore Women’s health conference.

Chef Dalton Fong, Cluster Head Chef of LINO, Singapore, will also be working with GloW for their upcoming diet and lifestyle intervention trial, which aims to improve women’s cardio metabolic profile and gut microbiome using an Asian-forward Mediterranean diet.

Themed “Promoting Women’s Health and Healthy Longevity: from Laboratory TO KITCHEN”, the conference gathered leading international and local scientists, experts, and practitioners in women’s health, maternal and child health, healthy longevity, public health, omics technology, and nutrition together to examine the myriad and unique health challenges women face across their lifespan, including

cardiometabolic health, cancer, and more.

From topics on fetal and maternal health to diet and nutrition, the discussions homed in on the associations between healthy dietary patterns and major women’s health and reproductive health outcomes such as pregnancy complications, risk of infertility, type 2 diabetes, cardiovascular disease and cancer. The three-day conference spanned a wealth of riveting discussions that added heft and direction to the current conversation on women’s health.

The conference also touched on the role of omics in the etiology and prevention of diseases. Some topics include how metabolomics and microbiome can facilitate personalised dietary assessments and intervention strategies for health, as well as their role in the prediction of maternal and reproductive health outcomes.

One conference highlight for a programme that looked at advances in food technology, mindful eating and sustainable menus saw Chef Mai Pham from California conducting an on-site cooking demonstration to showcase several easy and palatable dishes using ingredients common to an Asian diet.

Left: Prof Zhang Cuijin, Founding Director of GloW at NUS Medicine.

Middle: Prof Michelle Williams, Former Dean of the Harvard T.H. Chan School of Public Health, highlighted the importance of prioritising and investing in women’s health and well-being.

Right: Prof Frank Hu, Chair of the Department of Nutrition, Harvard T.H. Chan School of Public Health, provided valuable insights into eastern and western dietary patterns, underscoring their respective health advantages.



Bringing a Healthy Lifestyle and Diet to the Fore

As a preview to the Women's Health Conference from 9 to 11 November 2023, the Women's Health Conference – Healthy Lifestyle Coaching On-Campus Workshop held on 8 November 2023 at NUS Medicine, piqued the interest of the attendees with the benefits of a plant-forward diet for both the health of individuals and the planet, a tasty reward at the end of the session, and more.

Introducing the two main themes of the conference, lifestyle and nutrition, the workshop featured talks on fitness and active living, healthy eating, by renowned speakers Ms McKenna Smet, Certified Strength &

Conditioning Specialist, US, and Mr Greg Drescher, Senior Advisor of Strategic Initiatives at The Culinary Institute of America (CIA).

Proving that healthy eating can be both innovative and delicious, US-based Chef Mai Pham wielded her expertise and demonstrated the steps to her signature Shrimp and Watermelon dish which members of the audience enjoyed.

Concluding the session on a promising note, the panel discussion comprising Associate Professor Verena Tan from the Singapore Institute of Technology, Chef Dalton Fong, Cluster Head

Chef of LINO, Singapore, Chef Mai Pham, Owner of restaurants Lemon Grass (Sacramento) and Star Ginger, and Mr Greg Drescher delved into the possibility of a plant-forward diet in Singapore, the benefits and challenges, as well as how institutions and restaurants can play a part.



Ms McKenna Smet, Certified Strength & Conditioning Specialist, US, shared about the use of novel technology to understand and promote physical activity, as well as the impact of food consumption and exercise.



(From left to right) Associate Professor Verena Tan from the Singapore Institute of Technology, Chef Dalton Fong, Cluster Head Chef of LINO, Singapore, Chef Mai Pham, Owner of restaurants Lemon Grass (Sacramento) and Star Ginger, and Mr Greg Drescher, Senior Advisor of Strategic Initiatives at The Culinary Institute of America (CIA) delved into the possibility of a plant-forward diet in Singapore.

Scan to see the highlights of the conference





Responding at pace to Climate Change: Developing Innovative Strategies to Deliver Low-carbon, High-value Care

BY ALSTON NG, RESEARCH ASSISTANT, CENTRE FOR SUSTAINABLE MEDICINE

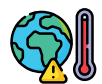
According to the 2023 Lancet Countdown report, The multiple and simultaneously rising risks of climate change are amplifying global health inequities and threatening the very foundation of human health. Health systems are increasingly strained, and 27% of surveyed cities declared concerns over their health systems being overwhelmed by the impact of climate change.¹

Given the accelerating pace of global climate change, health systems have the urgent task of transforming clinical practice, strengthening the climate-resilience of their facilities and services and delivering on healthcare decarbonisation.

Globally, healthcare provision accounts for 5-8% of carbon emissions. Were it a country, healthcare would be the fifth largest emitter on the planet. Aside from round-the-clock hospital operations, energy-intensive medical equipment use, and the reliance on single-

use disposables for infection control, certain medical practices magnify the carbon footprint of the healthcare sector.

Take the use of anaesthetic agents like desflurane and sevoflurane for instance. Both have a global warming potential many times that of carbon dioxide and they remain unmetabolised when released into the atmosphere. Desflurane, for instance, is 2,540 times more potent than an equivalent mass of carbon dioxide at trapping heat; using just a bottle produces the same effect as burning 440kg of coal.



27%

of surveyed cities declared concerns over their health systems being overwhelmed by the impact of climate change

5-8%

of carbon emissions are accounted for by healthcare provision

The potential for emission reductions in the healthcare sector is enormous. To support international efforts in climate action and maximise the co-benefits of healthcare decarbonisation, the Centre for Sustainable Medicine was launched in Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine). It sets out to:

- Pioneer clinically relevant and solutions-focused research designed to drive high-quality, low-carbon care.
- Transform medical education and prepare future healthcare professionals to be at the forefront of the response to climate change. This will involve embedding sustainability into the foundations of undergraduate medical school and graduate-level training opportunities for healthcare professionals of all backgrounds.
- Support health policymakers and hospital administrators across the world to develop effective strategies to achieve net-zero healthcare.

The Centre is led by Professor Nick Watts, who has been appointed Professor of Sustainable Medicine, and was Chief Sustainability Officer at the UK's National Health Service.

“Without urgent action, climate change will overwhelm health systems in Singapore and across the world. The newly minted Centre for Sustainable Medicine at NUS Medicine will tackle this challenge, helping doctors, nurses and hospitals prepare for the spread of infectious diseases and weather extremities. At the same time, it will conduct research and implement net

zero healthcare across the country, directly improving the health of our patients and reducing stretched health budgets,” said Prof Nick Watts.

A robust response to the climate crisis must be one that takes place at every level. Beyond modifying behaviour in care provision, health systems must develop innovative models and approaches to care that are patient-centred, energy-efficient, and non-polluting. This cannot be achieved without collaboration, dialogue, and learning between stakeholders

in climate science, public health, clinical practice, and healthcare administration.

To that end, the Centre attended the 28th session of the UN Climate Change Conference (COP28) as a representative of NUS and Singapore. There, it provided input to government officials, researchers, educators, and civil society leaders on the co-benefits of health-centred adaptation efforts and low-carbon care provision, and highlighted concrete first steps that health systems can adopt to deliver environmentally sustainable care.

Centre for Sustainable Medicine leadership Prof Nick Watts (2nd from left, back row) and Dr Amanda Zain (4th from right, front row) with NUS President, Professor Tan Eng Chye (3rd from left, front row) and the rest of the NUS delegation at COP28.



Without urgent action, climate change will overwhelm health systems in Singapore and across the world. The newly minted Centre for Sustainable Medicine at NUS Medicine will tackle this challenge, helping doctors, nurses and hospitals prepare for the spread of infectious diseases and weather extremities. At the same time, it will conduct research and implement net zero healthcare across the country, directly improving the health of our patients and reducing stretched health budgets.”

Prof Nick Watts

Come March this year, the Centre will also host the first in-person meeting of the newly formed Lancet Commission on Sustainable Healthcare in NUHS. Bringing together the world's leading experts on health, healthcare, and climate change, the Centre will advance the research agenda on sustainable care delivery and propose locally relevant strategies to achieve zero-carbon healthcare.

In the year ahead, the Centre will convene experts from the UK, US, Australia, and Singapore to develop the first comprehensive assessment of the carbon impact of healthcare in Singapore. Results from the assessment will inform future policies and standards in healthcare delivery, and allow experts to develop a well-rounded net-zero healthcare strategy to support Singapore in achieving its climate ambitions.

The field of sustainable medicine offers exciting opportunities for the healthcare profession to significantly improve health outcomes and strengthen health system operations. The good news is that support for climate action among healthcare professionals is already considerably high. In a survey conducted by the Centre, 82% of local healthcare professionals support action towards a more sustainable health system, and two-thirds believe that Singapore should participate in or be a role model for the international community in sustainable healthcare.

From global consensus on climate action to enthusiasm among local healthcare

professionals for sustainable medicine, the stage is set for a transformation in and thoroughgoing rethinking of healthcare provision. The Centre for Sustainable

Medicine looks forward to working with healthcare professionals of all backgrounds in creating a more sustainable health system for all.

The Centre for Sustainable Medicine at NUS Medicine was launched on 1 December 2023. It aims to establish a new field of medicine to accelerate the net zero transition in healthcare and support health systems in preparing for the worst impact of climate change.

How will the Centre for Sustainable Medicine achieve this?

EMPOWER clinicians with evidence and research

- Drive adoption of environmentally preferable practices through development and dissemination of clinically relevant guidelines, focusing first on volatile anaesthetics, inhalers, circularity in medical devices, and remote care and patient transport.
- Map footprint of key patient journeys and identify clinical substitution opportunities.
- Coordinate and grow the field of sustainable medicine in NUS and globally through industry networks, annual conference/lecture series, and a visiting professor-in-residence scheme.

ENHANCE health system development

- Advance common standards and approaches to carbon footprinting clinical products, pathways, and systems.
- Carry out a full assessment of the Singapore health system's carbon footprint and develop a high-level decarbonisation strategy for meeting Singapore's 2050 net-zero commitment.
- Provide bespoke services to healthcare providers, industry partners, and government agencies in research and strategy development on health systems adaptation and decarbonisation.

EDUCATE and **EQUIP** future healthcare leaders

- Embed sustainability in undergraduate medical programme.
- Offer advanced learning opportunities to mid-career and senior healthcare professionals in Singapore and across the region.
- Conduct training with healthcare professionals on pioneering low-carbon care interventions and advancing sustainable quality improvement at their workplaces.



¹ Romanello, Marina, Claudia di Napoli, Carole Green, Harry Kennard, Pete Lampard, Daniel Scamman, Maria Walawender, et al. "The 2023 Report of the Lancet Countdown on Health and Climate Change: The Imperative for a Health-Centred Response in a World Facing Irreversible Harms." *The Lancet* (2023). [https://doi.org/10.1016/S0140-6736\(23\)01859-7](https://doi.org/10.1016/S0140-6736(23)01859-7).



MEGICal Moments at NUS Medicine Educators' Day 2023

BY HAZWANI MOHAMED, MANAGEMENT ASSISTANT OFFICER, NUS MEDICINE DEAN'S OFFICE (EDUCATION)

Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) and the National University Health System (NUHS) recently held a series of events to celebrate education and our educators. This month-long celebration came to a close on NUS Medicine Educators' Day, on which eight finalist teams shared ideas with a panel of esteemed judges.

The Medical Education Grand Innovation Challenge (MEGIC) aims to provide a platform for educators and students to come up with creative solutions to enhance medical learning and teaching.

“Advancing health is not possible without new ideas, curiosity and science,” said Professor Chong Yap Seng, Dean of NUS Medicine.

This year's keynote speaker, Dr Siah Chiew Jiat Rosalind, Undergraduate Programmes Director for clinical education at the Alice Lee Centre for Nursing Studies at NUS, and a nurse clinician for community and gerontology at Singapore General Hospital, shared about the transformation of nursing education and how Artificial Intelligence (AI), etc., will be playing a pivotal role in shaping the future of healthcare.

MEGIC 2021 Special Mention Award winners, Team COMM-potent, shared about what went into creating their project and the challenges they faced. They started off with a problem statement: The medical student curriculum does not teach students how to communicate with people with disabilities. To tackle this problem, the team created the Communications with Persons with Disabilities Workshop to engage people with disabilities as patient educators to teach medical students how to effectively and sensitively communicate with them. Fast forward to today, the workshop has become a

regular fixture within the NUS Medicine curriculum. This year’s Medical Education Grand Innovation Challenge (MEGIC) saw an array of presentations including a podcast and a live simulation by the eight finalist teams. They presented their ideas to a panel of attentive judges—Professor Paul John Gallagher, Deputy Head Clinical at NUS department of Pharmacy, Associate Professor Soo Yuen Jien, Director of the Centre for Development of Teaching and Learning, and Associate Professor Seow Teck Keong, Deputy Director of The Centre of Development of Teaching and Learning.



Advancing health is not possible without new ideas, curiosity and science.”

Prof Chong Yap Seng, Dean of NUS Medicine



First Prize



First prize winners Team ReVISUALize won with their idea to teach smartphone ophthalmoscopy as a novel method of fundus examination to healthcare students. With this, they hope to address limitations and confer further benefits of digitisation for both learning and clinical practice.

Team members: Professor Louis Tong, Mr Benjamin Paik, Mr Bryan Tho Zhe Lun, Mr Maverick Wong Wenhao, Mr Tan Tuan Hao, Dr Loo Jin Liang, Associate Professor Khyber Alam, Associate Professor Kendrick Co Shih



Second Prize



Team TESLA-G (*Telegram Education for Surgical Learning and Application – Gamified*) emerged as second prize winners for their gamified, Telegram-delivered, quizzing platform for surgical education of medical students. It will also be a protocol for a pilot randomised controlled trial.

Team members: Mr Ang Yi-An, Mr Ng Song Peng, Matthew, Mr Ng De Rong, Tony, Dr Chia Jeng Long, Mr Craig Tan Jia Wei, Mr Wong Yee Howe, Dr Clement Chia Luck Khng, Assistant Professor Lorainne Tudor Car, Mr Ahmad Ishqi Jabir, Dr Dinesh Carl Junis Mahendran, Dr James Lee Wai Kit



Special Mention Award



Team The Knife Life started a surgery podcast which aims to enhance the learning for medical school undergraduates on surgical topics, prepare for surgical rotations/internships and help students revise prior to their examinations.

Team members: Dr Serene Goh Si Ning, Ms Clarisse Hing, Mr Elliott Lee Ying Hao, Ms Kathleen Ann Pang, Ms Rachel Goh, Ms Selvie Yeo, Ms Victoria Zheng, Dr Caleb Ng Wei Hao, Dr Ho Wei En, Dr Lydia Tan, Dr Ng Ding Rui, Aubrey, Dr Phoebe Aw, Dr Woon Chang Yi, Dr Zhao Jiashen



Third Prize



Team MasterRAD won the third prize with their idea to master Radiological Anatomy through interactive, competitive and educational gameplay.

Team members: Dr Wynne Chua, Mr Chia Koon Liang, Ms Joanne Hang, Mr Shawn Low, Dr Li Zongchen, Dr Ong Shao Jin, Dr Samuel Lau



Best Video Award

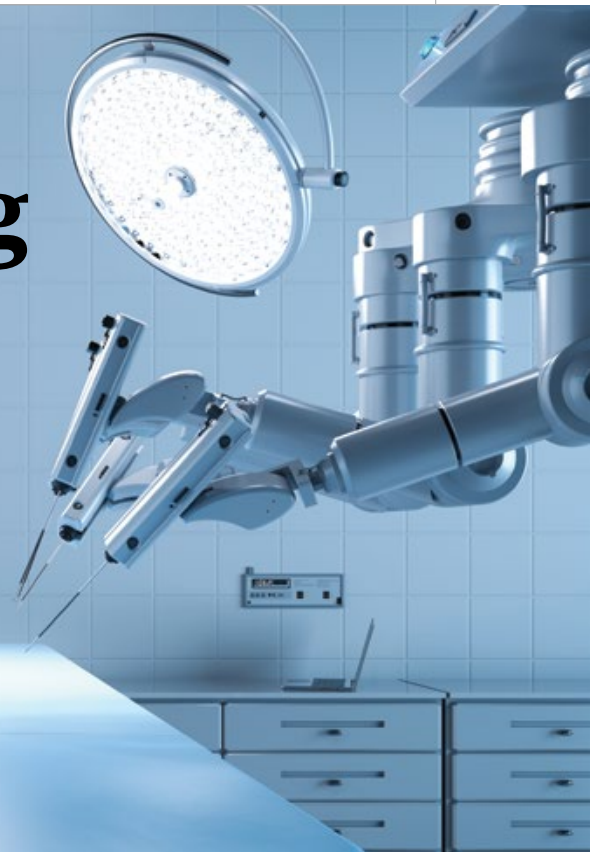


Team HabIT clinched the award with their High-fidelity Virtual Reality (VR) simulation for Augmentation of Basic Cardiac Life Support In First Responder Training in Out-of-Hospital Cardiac Arrests (HABIT- OHCA).

Team members: Ms Surabhi Riya Vig, Mr John Yap Yin Gwee, Mr Lin Yibin, Mr Mak Hon Keat, Dr Ada Ngo, Dr Chionh Wen Wei, Dr Crystal Soh Harn Wei, Dr Darius Pan Shaw Teng, Adjunct Professor Malcolm Mahadevan



Groundbreaking Telesurgery Trial Spanning Over 5,000km



In an extraordinary fusion of technology and medical expertise, clinician-scientists from Singapore and Japan embarked on an exciting new collaboration—robotic telesurgery, aided by recent developments in advanced surgical robots and network telecommunication technology.

Picture this: in a sterile operating room in Nagoya, Japan, robotic arms move with astonishing precision as they prepare to perform a complex laparoscopic surgical procedure.

What makes this scenario truly remarkable is the surprise twist—it's not the surgical team in Nagoya controlling these robotic arms. Instead, they are being orchestrated by surgeons located over 5,000km away in the Advanced Surgery Training Centre at Singapore's National University Hospital (NUH), the

teaching hospital of the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine).

NUS Medicine and NUH collaborated with Fujita Health University (FHU) in its first robotic telesurgery trial between Singapore and Japan, from 9 to 11 October 2023. Leveraging Japan's first surgical robot, clinician-scientists from NUH and NUS Medicine remotely performed a gastrectomy (stomach surgery performed for cancer) on a simulated organ from a surgeon cockpit in Singapore.

The surgeons' movements were transmitted, directed, and replicated by a robotic operation unit located in Japan via a dedicated international fiber-optic network.

This collaboration follows the Memorandum of Understanding (MOU) signed in August 2023 between NUS Medicine and FHU, one of Japan's leading universities with a strong research focus in robotic surgery and telesurgery. The MOU aims to deepen academic partnership through active joint collaborations, including the execution of remote surgical experiments, and promote mutual exchange activities such as student exchange programmes.

Harnessing the potential of telesurgery

The two gastric surgeons leading the demonstration in Singapore are Professor Jimmy So from the Department

of Surgery, NUS Medicine, and Senior Consultant in the Department of Surgery, NUH, as well as Assistant Professor Kim Guowei from the Department of Surgery, NUS Medicine, and Consultant in the Department of Surgery at the NUH.

In Japan, the surgical team is led by Professor Ichiro Uyama and Professor Koichi Suda from FHU.

The preclinical trial—involving a series of complex gastrectomy procedures conducted by both teams—aims to prove that long-distance robotic telesurgery for technically demanding procedures can be safely conducted using a robotic system connected by high-speed fiber-optic communication.

While robotic surgery is not new in Singapore, this collaboration between NUS Medicine, NUH and FHU marks a critical step towards making remote surgeries an accessible option to patients in the near future.

“Remote telesurgery offers immense potential to enhance global access to specialised care, reduce travel and wait times for patients, minimise health risks during emergencies and pandemics, and foster training and collaboration among medical professionals worldwide. It also contributes to improved surgical expertise for complex cases, particularly benefitting underserved areas,” said Prof Jimmy So, lead of the surgical team in Singapore.

During public health crises, such as a global pandemic, remote telesurgery helps minimise the risk of disease transmission between patients, healthcare workers, and surgical teams. Surgeons can



Remote telesurgery offers immense potential to enhance global access to specialised care, reduce travel and wait times for patients, minimise health risks during emergencies and pandemics, and foster training and collaboration among medical professionals worldwide. It also contributes to improved surgical expertise for complex cases, particularly benefitting underserved areas.”

Prof Jimmy So, Surgical Team Lead in Singapore



perform surgeries from a safe location, reducing the potential for infection spread. Such forms of surgery also help promote tele-mentoring or distance learning in medical education, allowing young doctors and medical students to learn surgical techniques and skills from lecturers and medical experts based not only in a different part of Singapore, but also anywhere in the world.

Assistant Prof Kim Guowei added, “In partnering with our Japanese colleagues, we

hope to advance and unlock the potential of telesurgery for patients and doctors alike. This continuous exchange of knowledge, advanced surgical techniques, and best practices across borders contributes to improving surgical expertise and outcomes.”



(From left) Prof Koichi Suda, Prof Ichiro Uyama, Dr Kim Guowei and Prof Jimmy So (seated) are the four gastric surgeons leading the gastrectomy demonstration, a collaboration between NUS Medicine, NUH and Fujita Health University. (Photo Credit: National University Health System)



Scan to watch the surgery in action

The Future of Medicine: Revolutionising Healthcare with Digital Solutions

A new book written by researchers from the Institute for Digital Medicine (WisDM) at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) describes digital solutions as a new way to help patients manage symptoms for pain, diabetes, hypertension, cancer and more.

Photo:
"Medicine Without Meds: Transforming Patient Care With Digital Therapies", written by researchers at WisDM, NUS Medicine

Some patients with sleep disorders, back pain, diabetes, cancer, and attention-deficit/hyperactivity disorder are benefitting from digital health interventions that use software programs, often delivered through mobile apps or web-based platforms, to treat, manage, or prevent a medical condition. Designed to provide therapeutic benefits backed by clinical evidence, these digital interventions often complement traditional healthcare approaches.

"Medicine Without Meds: Transforming Patient Care With Digital Therapies" showcases this new approach, believed to be one of the most promising avenues for improving patient outcomes and the provision of healthcare on a global scale. It also provides a much-needed blueprint for accelerating digital innovation to patients.

While relatively new in the healthcare arsenal, digital therapeutics or DTx, is a new class of medicine akin to drugs. According to the book's three authors, DTx has the potential to revolutionise patient care by improving access to healthcare, personalising treatment, and increasing convenience in achieving better health.

Written by researchers from WisDM at NUS Medicine, the book provides actionable ways of bringing digital therapy to fruition and inspiring new AI-driven innovations that could revolutionise the future of medicine.





“Our vision is to build good digital solutions that are also cost-efficient and sustainable in the long run. From the birth of an idea to its successful implementation, it is critical to engage the key stakeholders closely, including patients, clinicians and investors. The book offers a roadmap on how digital innovation can be developed and implemented effectively, to serve patients, caregivers, and those who may not be in ill health and want to get better,” said Prof Dean Ho, WisDM’s director and one of the book’s three co-authors.

Since the team was formed in 2018, researchers have developed digital health solutions to help a patient with advanced prostate cancer who was recommended a 50% reduction in dose of an investigational inhibitor drug for increased efficacy, and subsequently resumed an active lifestyle. In a larger cohort of solid cancer patients, personalised treatment with the CURATE.AI platform saw a marked reduction of nearly 20%

on average. This digital solution was widely featured at the prestigious American Society of Clinical Oncology (ASCO) Annual Meeting and the ASCO Educational Book. The team also leveraged DTx to address ageing and illness-related challenges in cognitive and physical performance, such as brain cancer and cognitive decline.

In one of the team's latest DTx projects, conducted in collaboration with local technology and service providers, an application is currently undergoing validation. The app assists patients with hypertension in managing their condition by tracking body vitals, including blood pressure and heart rate, all with just a phone’s camera. Mrs Jenny Pek, 77 years old and a participant of the ongoing study, said, “My doctor has advised me to monitor my blood pressure regularly, and I can easily do that with the help of the app. It provides me useful tips and recommendations that help me keep my diabetes under control.”

Co-author Mr Yoann Sapanel, Head, Health Innovation, WisDM, NUS Medicine, said, “DTx offers a high degree of personalisation tailored to an individual's needs and progress. They adapt to the user's specific condition by collecting valuable data on patient progress, which not only benefits patients but also aids healthcare providers in optimising treatment plans, enabling data-driven insights and informed decision-making for the most effective personalised treatment.”

Dr Agata Blasiak, Head, Digital Health Innovation, WisDM, NUS Medicine, is the third author. She said, “DTx plays an important role for Singapore and beyond, as it can allow for decentralised delivery of healthcare at home, for certain conditions. With DTx that can remotely deliver treatment and monitor outcomes, patients need not always visit the clinics or hospitals, and the overall costs of healthcare can be reduced. DTx often works by providing rewarding interactions and nudges through



(From left) Yoann Sapanel, Dr Agata Blasiak, D.A. Wallach, Poonam Rai, Prof Dean Ho, and Prof Chong Yap Seng, Dean of NUS Medicine, celebrating the launch of a new book by WisDM, NUS Medicine.

mobile apps, to empower patients to understand and take charge of their condition, make lasting changes in their lifestyle and develop habits for better health and a better life.”

Published as a trade book by the Johns Hopkins University Press, the oldest continuously running University Press in the United States, the book's foreword is written by American musician and business executive D.A. Wallach, who is passionate about technologies poised to reinvent the practice and delivery of medicine. It also features contributions and insights from various entrepreneurs, executives, patients and clinicians globally, including Associate Professor Ngiam Kee Yuan, Group Chief Technology Officer, National University Health System (NUHS) and Deputy Director of WisDM; Associate Professor Robyn Mildon from NUS Medicine's Centre for Holistic Initiatives for Learning and Development (CHILD) and Centre for Behavioural and Implementation Science Interventions (BISI), and Founding Executive Director of the Centre for Evidence and Implementation, Australia; Dr Eddie Martucci, CEO and Co-founder of Akili Interactive Labs, United States; and Owen McCarthy, President and co-founder of MedRhythms. The cover was artfully designed by Shian Ng, an acclaimed Singapore artist.

All author proceeds from the sale of the books will be donated to the WisDM Patient Impact Fund, to help patients in Singapore.



Scan for more information on the book

Book on Digital Medicine Launched by Grammy Award-winning Artiste-entrepreneur

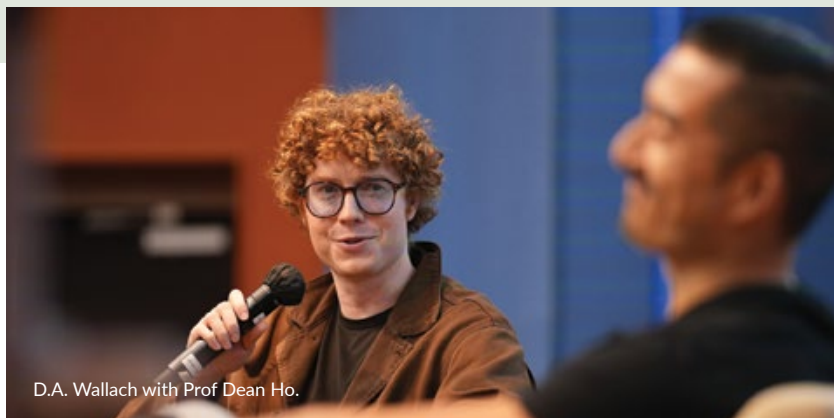
Artiste-technopreneur D.A. Wallach was in Singapore in November 2023 for the launch of “*Medicine Without Meds: Transforming Patient Care With Digital Therapies*”, for which he wrote the foreword. D.A. who is the co-founder of the non-profit Franca Fund for preventive genomics and General Partner of Time BioVentures gave his take on how to recognise the potential for rapid growth and scalability in small businesses.

“It starts with a spark of genuine passion. Occasionally, something stands out and we listen to our instincts. It starts with falling in love, and we then enter a very protracted process—where we evaluate every dimension of the risks associated with the project. After several rounds of assessments and conversations, we tend to have a better understanding of the risks and weaknesses of the plan. If we still want to invest in the business by the end of this process, that is when we go ahead to do it. It's a combination of being intuitive on one hand, but also rigorous and systematic on the other, so that we ensure diligence in the process and avoid making stupid mistakes.”

Curiosity and passion powered his itinerant life journey, from starting a rock band to pursuing his hobby

as a venture capitalist. An acclaimed recording artiste who has toured with Lady Gaga, Weezer, and Blink 182, acted in the film *La La Land* which received 14 Academy Award nominations, and performed on TV Shows including *Jimmy Kimmel Live* and *Late Night with Jimmy Fallon*, D.A. was named to the *Forbes'* inaugural 30 Under 30 in the music category in 2011. Since 2015, he has set out to build a career as a venture capitalist, backing a series of industry-defining technology companies including Spotify, SpaceX, Ripple, The Boring Company, and Memphis Meats.

Echoing a theme from the book, D.A. said healthcare systems need to identify and train people who can work well in collaboration with technology and software. “Having encyclopaedic memory is not what will matter to the physicians of the future. Instead, it will be the ability to rapidly access information to enable, among other things, identifying patients with rare diseases. Today, too many patients go on diagnostic odysseys because no one can pattern-match their disease with what was learned in medical school or seen clinically. We have an opportunity now with technology to give humans a lot more leverage—and I think that will be the crux of the future.”



D.A. Wallach with Prof Dean Ho.

Nano-sized Cell Particles Are Promising Intervention Tools in Treating Infectious Diseases

In a study led by researchers at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), extracellular vesicles were found to inhibit the viral infection of COVID-19 and potentially other infectious diseases

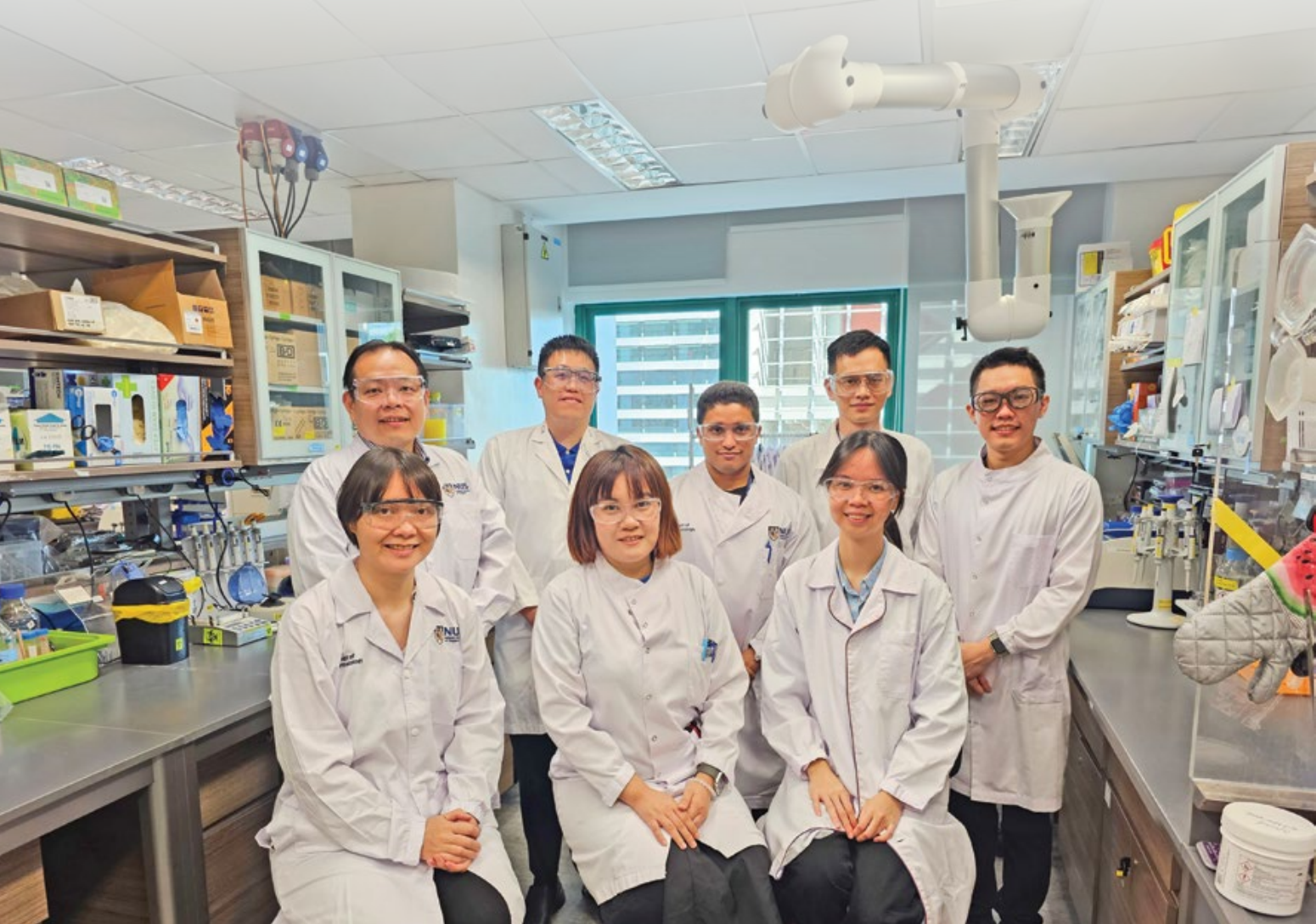
Photo:

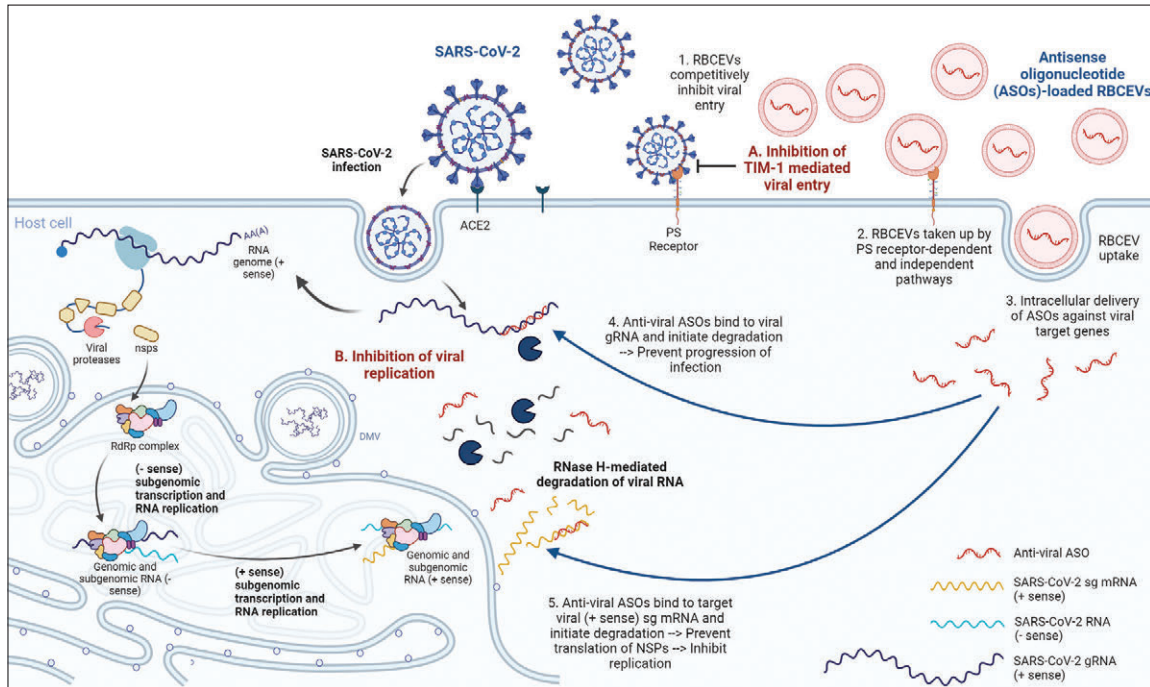
Authors of the study, from NUS Medicine: (From left) Migara Jayasinghe, Brendon Zhi Jie Yeo, Assoc Prof Justin Chu, Dr Kai Sen Tan, Dr Dai Cao Phung, Rebecca Carissa Prajogo, Gao Chang, Asst Prof Minh Le.

The COVID-19 pandemic demonstrated the importance of being prepared with drug interventions to contain viral outbreaks that can otherwise have devastating consequences. In preparing for the next pandemic—or Disease X, there is an urgent need for versatile platform technologies that could be repurposed upon short notice, to combat infectious outbreaks.

A team of researchers, led by Assistant Professor Minh Le

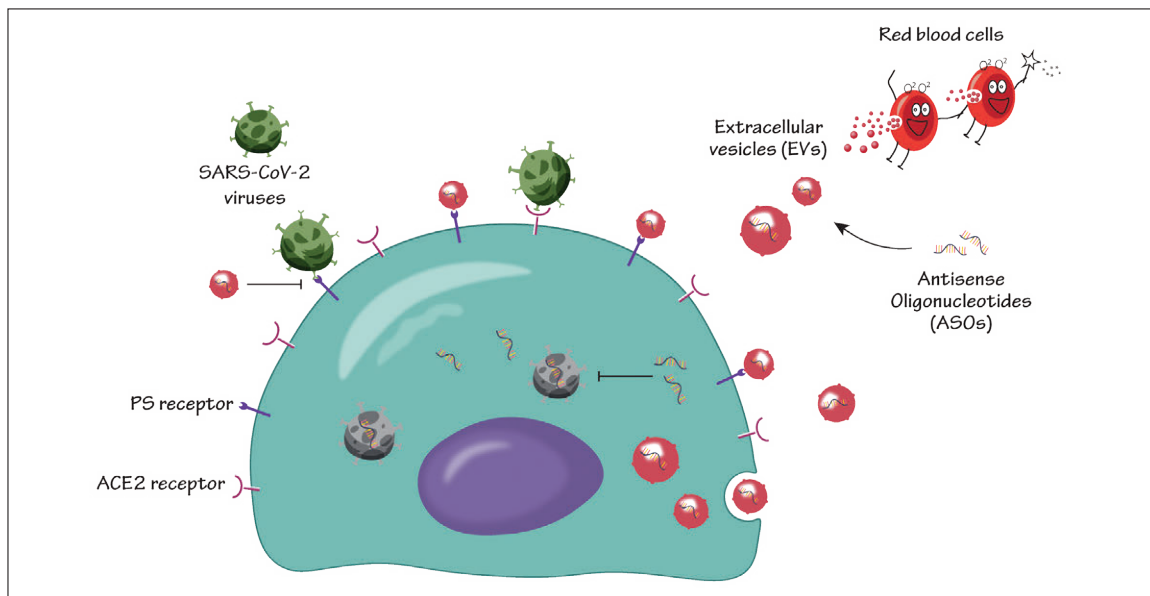
from the Institute for Digital Medicine (WisDM) and Department of Pharmacology at NUS Medicine, discovered that nano-sized particles released by cells, termed “extracellular vesicles” (EVs), can curb the viral infectivity of SARS-CoV-2—its wild type and variant strains—and potentially other infectious diseases. Asst Prof Le said, “Our study showed that these cell-derived nanoparticles are effective carriers of drugs that target viral genes precisely. These EVs are therefore efficient





←
Top:
 Mechanism of extracellular vesicle (EV)-mediated SARS-CoV-2 inhibition.
 Credit: Migara Jayasinghe.

Bottom:
 Inhibition of SARS-CoV-2 virus infection by red blood cell extracellular vesicles (RBCEVs).
 Credit: Trinh Tran.



tools for therapeutic intervention in patients who are infected with COVID-19 or other infectious diseases.”

The study, conducted in collaboration with NUS Medicine’s Biosafety Level 3 (BSL3) Core Facility, the Cancer Science Institute of Singapore, and the School of Physical and Mathematical Sciences at Nanyang Technological

University (NTU), demonstrated potent inhibition of COVID-19 infection in laboratory models using a combination of EV-based inhibition and anti-sense RNA therapy mediated by *antisense oligonucleotides* (ASOs). A versatile tool that can be applied to any gene of interest, ASOs can recognise and bind to complementary regions of target RNA molecules and induce their inhibition and degradation.

In the study, published in *ACS Nano*, the authors utilised human red blood cell-derived EVs to deliver ASOs to key sites infected with SARS-CoV-2, resulting in efficient suppression of SARS-CoV-2 infection and replication. The researchers also discovered that EVs exhibited distinct antiviral properties, capable of inhibiting phosphatidylserine (PS) receptor-mediated pathways of



Rebecca Carissa Prajogo, one of the study's researchers, performing an assay to quantify viral infection.

viral infection—a key pathway utilised by many viruses to facilitate viral infection. These viral inhibitory mechanisms were applicable to multiple variants of SARS-CoV-2, including the Delta and Omicron strains, ensuring their broad effectiveness against SARS-CoV-2 infection.

The results from the study point to anti-sense RNA therapy with ASOs as a potentially effective approach that could serve to combat future viral outbreaks. The platform that was developed to deliver ASOs through EVs to target the SARS-CoV-2 viral genes can be readily applied to treat other viral infections by replacing the ASO sequences with those complementary to the target viral genes. Asst Prof Le and her graduate students Migara Jay and Gao Chang, the first authors of the study, are currently developing more

potent combinations of ASOs with the help of artificial intelligence prediction models to achieve enhanced viral inhibition. This collaborative effort includes partnership with the research teams of Associate Professor Edward Chow from WisDM, NUS Medicine, and NUS Medicine's BSL3 Core Facility.

Associate Professor Justin Chu, Director of the BSL3 Core Facility at NUS Medicine, and co-author of the study, added, "This remarkable extracellular vesicle-based delivery platform technology coupled with anti-viral therapy is highly promising to combat a broad range of viruses and even Disease X." The latter is a general description for emerging and unknown infectious threats, such as novel coronaviruses. The term was used to alert and encourage the development of platform technologies, including

vaccines, drug therapies and diagnostic tests, which could be quickly customised and then deployed against future epidemic and pandemic outbreaks. Assoc Prof Chu is also from the Infectious Diseases Translational Research Programme at NUS Medicine.



This work brings the scalable and well-tolerated extracellular vesicle-based drug delivery platform an important step closer towards clinical validation studies."

Professor Dean Ho, Provost's Chair Professor and Director of WisDM at NUS Medicine

Game Changer for Future Production of Vaccines and Therapeutics to Fight Infectious Disease

A novel glycoengineering platform, created by the laboratory of Assistant Professor Chris Lok-To Sham from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), is poised to revolutionise future production of vaccines and therapeutics to fight infectious diseases.

Glycoengineering aims to manipulate sugars to produce useful carbohydrates. This innovative platform simplifies the customising and production of sugar carbohydrates known as glycans that play a crucial role in various therapeutic applications. Sugar-adding enzymes called glycosyl transferases (GTs) produce glycans and control the structural diversity of glycans.

The team found that the capsular polysaccharide (CPS), the sugar layer which encases many bacteria have extreme diversity, where its enzymes can be exploited to build many customised glycans. "These enzymes are like Lego. The more types of Lego bricks you have, the more unique types of glycans you can build," explained Asst Prof Chris Sham from the Department of Microbiology and Immunology at NUS Medicine.

Armed with this knowledge, Asst Prof Chris Sham and his graduate student Su Tong from the Department of Microbiology and Immunology, together with their team from the Infectious Diseases Translational Research Programme at NUS Medicine, took advantage of the diverse pathways of the bacterial CPS and the ease of modifying its pathways to create this novel glycoengineering

platform. This platform provides increased versatility in modifying GTs, facilitating the engineering of newly customised glycans.

Customised glycans, essential for diverse therapeutic applications, require a versatile platform capable of the insertion, deletion, substitution and general modification of glycan linkages. The team found that by relaxing the specificity of the precursor transporters, they could broaden the range of residues entering the cytoplasm. This innovation enables the production of customised glycans with unprecedented flexibility.

"The process of customising glycans, or glycoengineering, is made more challenging because it mostly relies on in-vitro approaches. These issues affect the efficient production of vaccines and other biological therapeutics. The new platform circumvents this challenge by demonstrating the possibility to genetically manipulate and engineer new glycans, giving rise to new knowledge about GTs, which ultimately signals an important advancement in glycoengineering," Su Tong said.

To date, the team has already celebrated significant achievements, including the



successful synthesis of clinically relevant glycans such as the Galili antigen, blood group antigens and Lewis antigens. These glycans can contribute to positive outcomes in the areas of organ transplants and blood transfusion when antibody rejection occurs in situations where the patient's blood group is incompatible with the donor and possibly result in severe inflammation and cell death.

Asst Prof Chris Sham is optimistic about the future development of this glycoengineering platform in creating more glycans for a broad variety of specific needs.

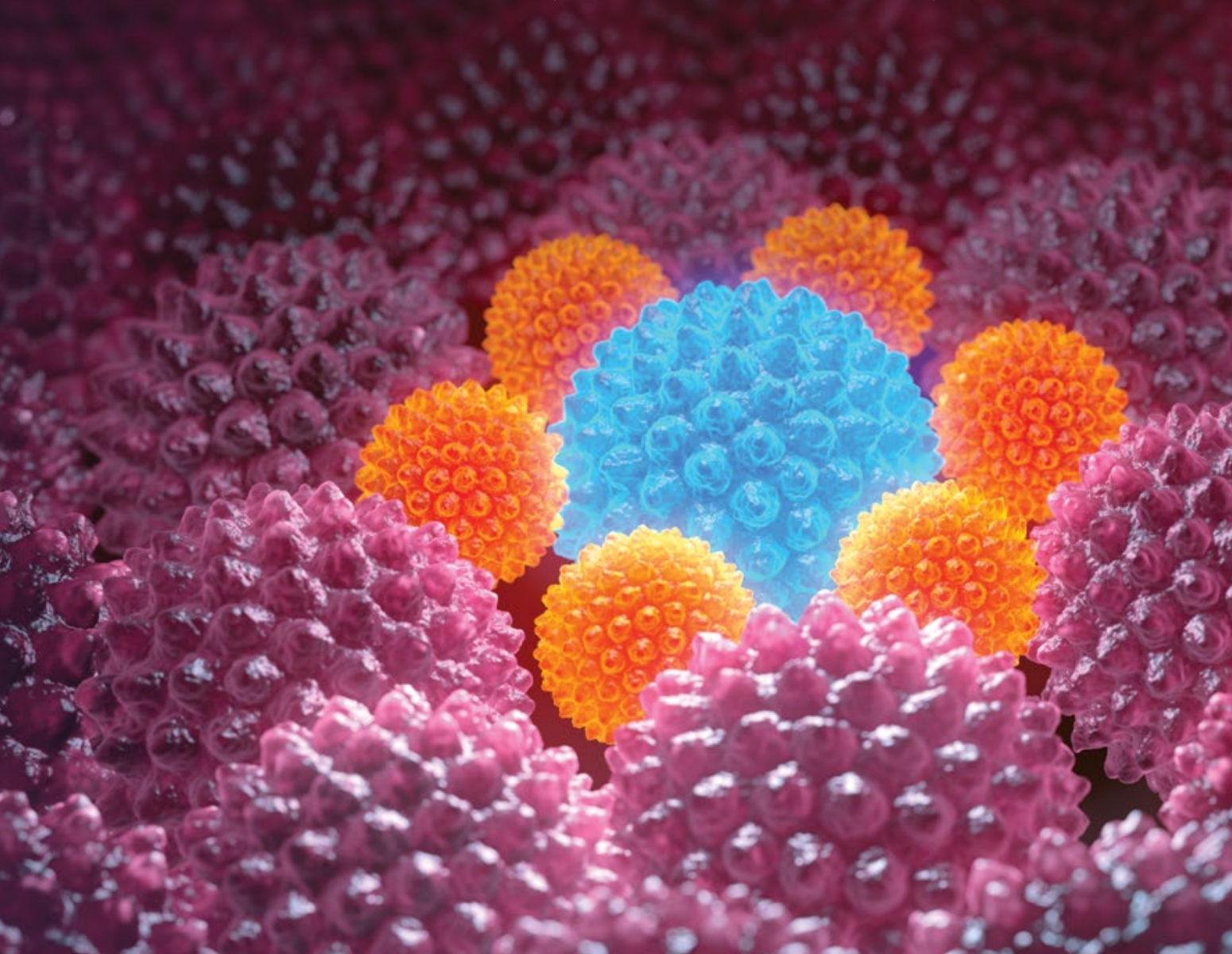
"The current focus is to make glycans found in mammals, but in the future the team hopes to use this novel platform technology and adapt it to multiple bacterial species to generate more useful carbohydrates for other applications, such as countering immunological paralysis and graft rejection," said Asst Prof Chris Sham.

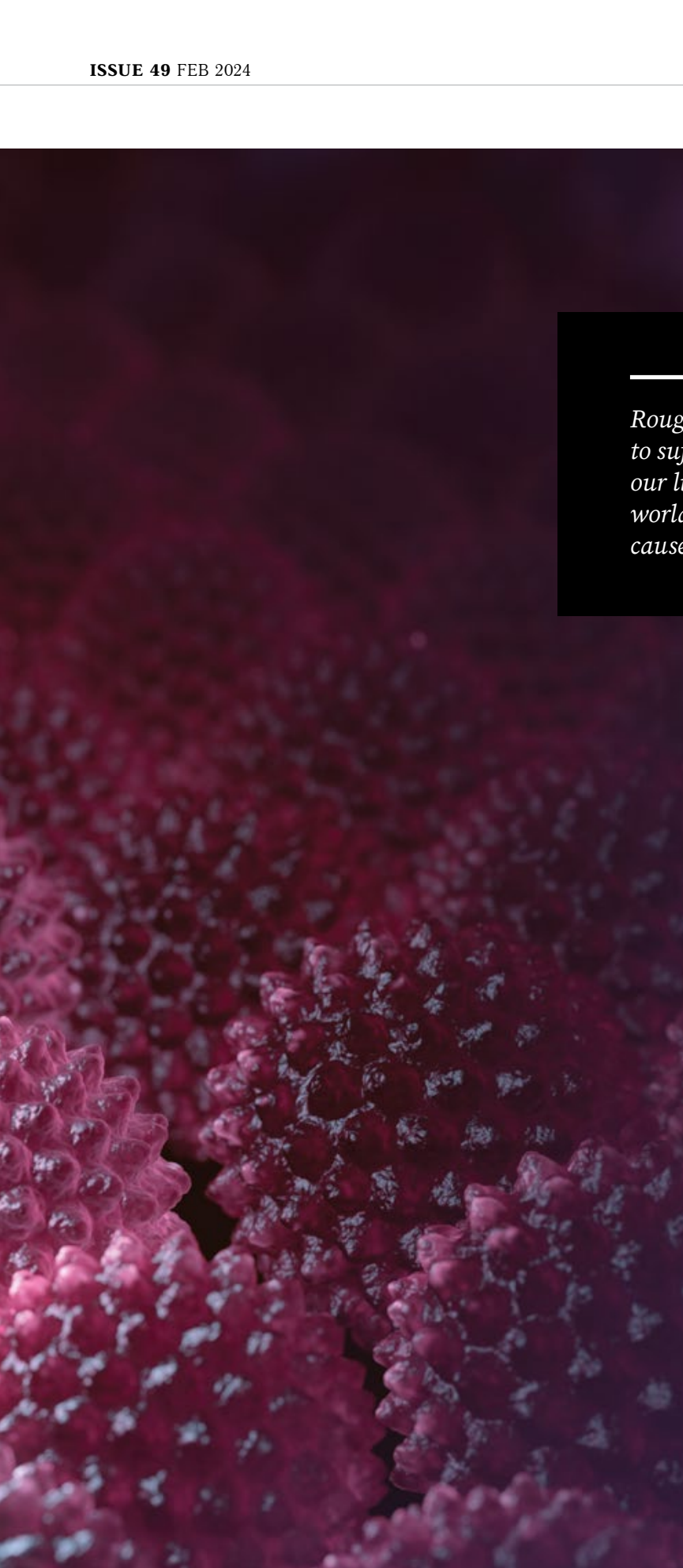


Scan to read the full paper here:

Why is Cancer so Hard to Treat?

BY DISTINGUISHED PROFESSOR ASHOK VENKITARAMAN, DIRECTOR, CANCER SCIENCE INSTITUTE OF SINGAPORE,
NATIONAL UNIVERSITY OF SINGAPORE & RESEARCH DIRECTOR, INSTITUTE FOR MOLECULAR AND CELL BIOLOGY, A*STAR



A large, detailed microscopic image of cells, likely cancer cells, showing their irregular, clustered structure. The cells are stained in shades of purple and pink, with some appearing more densely packed than others. The background is dark, making the individual cells stand out.

Roughly one in every three of us is expected to suffer from cancer at some point in our lives. Cancer incidence is increasing worldwide, and this disease is a leading cause of death amongst Singaporeans.

But cancer is not a singular disease. It can arise in almost any organ in our bodies, and at each site, with distinctive characteristics. For example, breast cancer is different from liver cancer or stomach cancer, and so on. For these reasons, cancer is best considered as a group of diseases rather than a singular entity.

When cells go rogue

Nevertheless, cancers arising anywhere have certain shared features, which come from the events that lead to cancer formation. We call this process “carcinogenesis”. During carcinogenesis, normal cells that make up different organs are transformed into cancer cells. So, for example, how is a normal liver cell different from a cancerous liver cell?

By and large, normal cells are well behaved, and play by inbuilt rules that keep us healthy. For instance, normal cells have a defined lifespan. Normal cells will not keep dividing to create daughter cells unless instructed to do so when necessary. Normal cells tend to stay in place, and do not invade other parts of the body.

Cancer cells break these inbuilt rules, and go rogue. They overcome limits on normal lifespan, and often continue to divide into daughter cells, forming a tumour (which is a term to describe swelling or new growth). Cancer cells invade other parts of the body, often distant from where the tumour was first formed.

What makes cancer cells break the inbuilt rules that keep us healthy? These inbuilt rules are encoded in our genes (which are

made from a molecule called DNA, present in each of our cells). During carcinogenesis, normal cells accumulate more and more faults in their genes. The growing number of faults cause the rules that govern normal cells to break down, transforming them into cancer cells. This process can be likened to the accumulation of faults over time in the memory of a computer, which eventually causes the computer to fail, because the instructions for its operation stored in the memory have been damaged. DNA in a similar way serves as a memory which carries instructions for normal cell behaviour encoded as genes—when faults accumulate in genes, normal cell behaviour breaks down, and normal cells can be transformed into cancer cells.

Simply understanding how cancers are formed, and how cancer cells are different

from normal cells, helps to explain why cancer is so hard to treat.

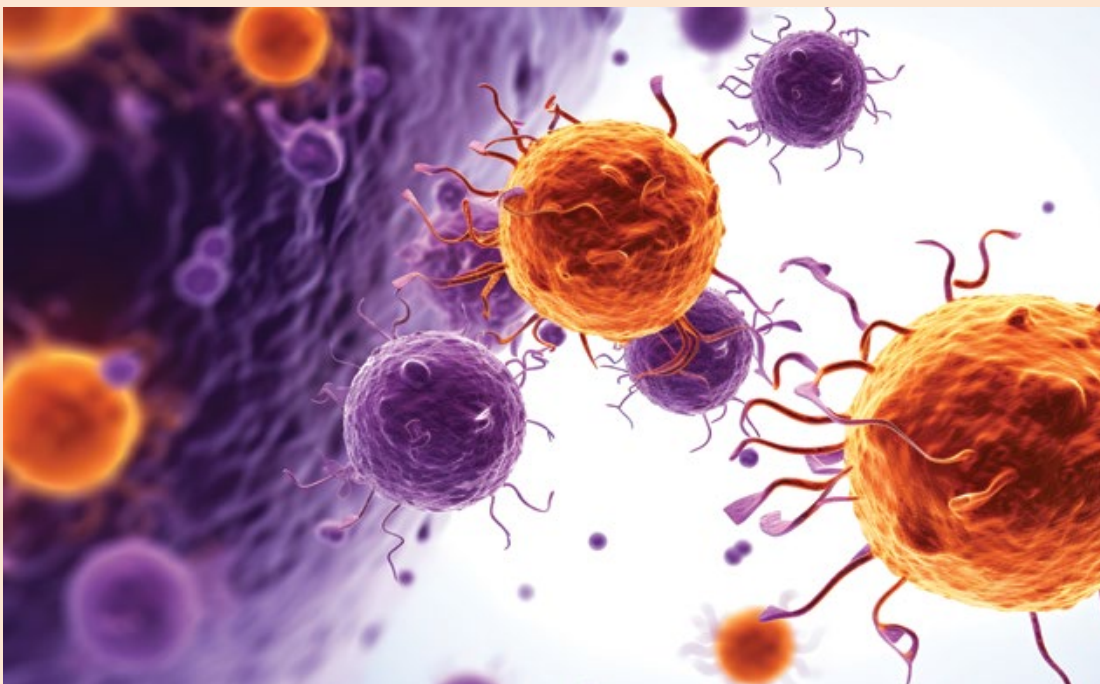
Total eradication of rogue cells is essential

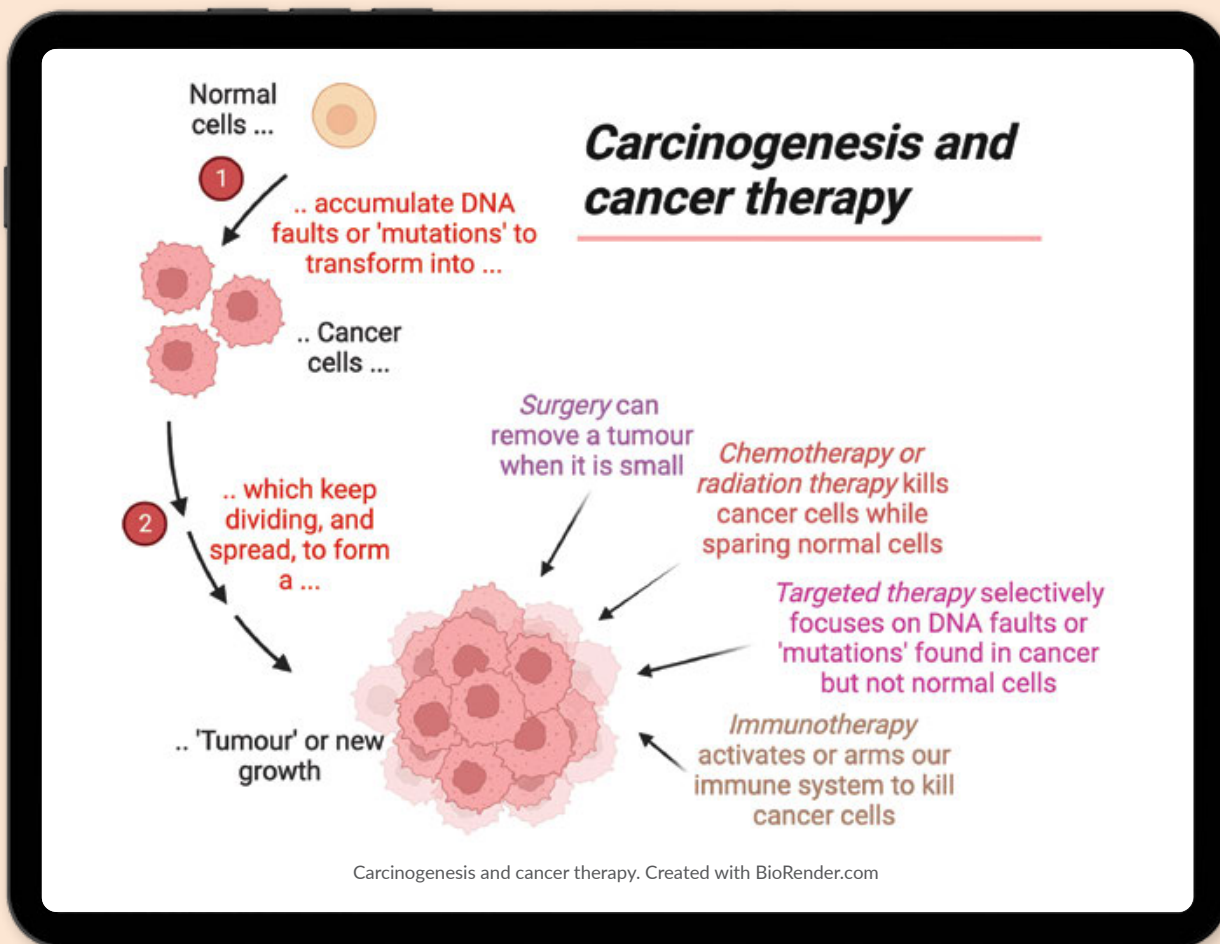
To cure cancer, we must completely remove or eliminate all—100%—of the rogue cancer cells. Getting rid of even 99% may not be enough, because cancer cells will often continue to divide into daughter cells, and the cancer could come back.

Sometimes—when cancer is detected in its earliest stages and is still small—surgery can remove the entire tumour. However, if even a small number of cancer cells is left behind, the cancer can come back. That is why surgeons must be very careful to completely remove the cancer, and why after surgery, patients are often monitored for several years to check if the cancer starts to come back.



Roughly
1 IN 3
individuals is
expected to
suffer from
cancer at some
point in their lives





Unfortunately, many cancers are too advanced at the time of diagnosis to be completely removed by surgery alone, and other treatments are required. Any effective treatment for cancer has to specifically target cancer cells, but leave normal cells unharmed. Cancer treatments attempt to achieve this goal by targeting features of cancer cells that are not shared with normal cells.

For example, cancer cells often divide whereas normal cells do not. Many treatments for cancer—like chemotherapy or radiation—tend to kill cells that are dividing rapidly.

So, cancer cells are more sensitive to these treatments than normal cells. However, the margin of sensitivity is not very high, and so treatments like chemotherapy or radiation also have side-effects on normal cells and cannot be given in very high doses. For this reason, it is often impossible to completely kill 100% of cancer cells using chemotherapy or radiation, making cancer difficult to treat.

To make matters worse, cancer cells often develop resistance to drugs or radiation. Such resistant cancer cells cannot be killed by these treatments, again making cancer difficult to treat.

“Sometimes—when cancer is detected in its earliest stages and is still small—surgery can remove the entire tumour. However, if even a small number of cancer cells is left behind, the cancer can come back. That is why surgeons must be very careful to completely remove the cancer, and why after surgery, patients are often monitored for several years to check if the cancer starts to come back.”

In addition, cancer cells unlike normal cells spread throughout the body. A cancer patient at the time of diagnosis may have cancers in many different parts of the body, and not just in one place. Such spreading makes it almost impossible to completely remove advanced cancers using surgery alone, and also makes cancer difficult to treat using drugs or radiation after it has spread widely.

Advances in treatment

What is being done to solve these problems and make cancer treatment more effective? There have been many important advances in recent years that offer increasing hope for cancer patients. Most cancers are now being treated using a combination of drugs, or drugs plus radiation. 'Combination therapy' has two main advantages. Combinations that kill cancer cells in different ways are often more effective than a single therapy. Moreover, drug resistance becomes less problematic,

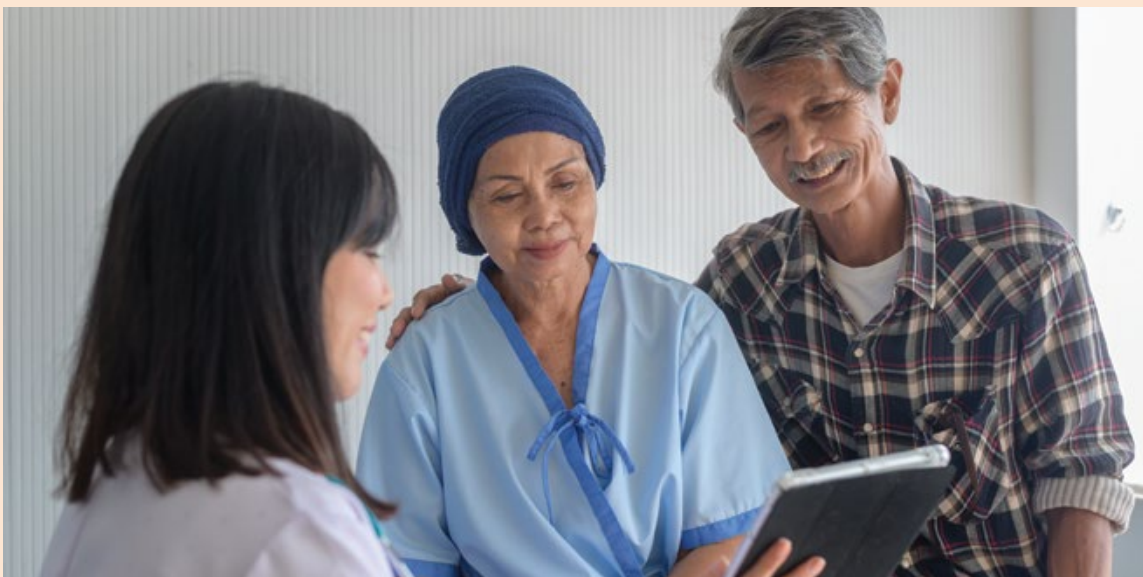
because the chance that cancer cells develop resistance to different kinds of therapy at the same time is low.

New modes of treatment that are more efficient at killing cancer cells and with fewer side effects, are being developed. It is now possible to 'read' the DNA in cancers, and pinpoint the faulty genes that cause the cancer. Very specific treatments—termed 'targeted therapy'—can be developed to selectively kill cancer cells carrying these faulty genes, while sparing normal cells. So, targeted therapy is more effective and has fewer side effects.

Cancer cells can evade our immune system by assuming a stealth mode in which they become invisible to the immune system, and thereby evade elimination. New therapies—called 'immunotherapy'—which reactivate the immune system against cancer have been developed. Some immunotherapies involve

drugs that make cancer cells visible to the immune system. Other immunotherapies arm our own immune cells to identify and kill cancer. These armed cells—called CAR-T or TCR-T cells—can be injected back into cancer patients to treat cancer. While immunotherapies are proving effective, they remain very expensive and often do not work for reasons that are not yet well understood.

Further research on cancer remains vital to overcome these problems. Over half of the world's population is of Asian descent, but most cancer research has been carried out on samples or models that reflect European descent. We have begun to appreciate that cancers in Asia can differ from cancers in other populations, and that different treatments may be required. This is one important reason for continuing cancer research in Singapore, to ensure that patients here can benefit from the latest advances.



Small Country, Large Research Trials – What Singapore Can Learn from Denmark

BY PROFESSOR JERRY MENIKOFF, CENTRE FOR BIOMEDICAL ETHICS, NUS YONG LOO LIN SCHOOL OF MEDICINE

Clinical trials generally require large numbers of participants, and that puts smaller countries like Singapore at a disadvantage when they join international trials with little to no say in how they are designed. However, smallness can also become an advantage.

Can getting an email with the right message convince someone to get an influenza vaccine? Researchers in Denmark set out to answer that question in 2022, with the ambitious goal of enrolling almost every Danish citizen aged 65 years or older in the Nudge-Flu clinical trial, and the answer was a resounding yes—almost one million participated in the Nudge-Flu trial that was conducted quickly and at very low cost.

The research team attributed that not only to the use of a mandatory governmental electronic letter system, but also to the fact that Denmark—with its relatively small population and high levels of trust in the government—has several electronic databases that maintain various types of information about its citizens that can be accessed efficiently, safely and at minimal cost.



How is this research relevant to Singapore? The short answer is that we could possibly be missing out on country- or culture-specific nuances.

Small countries can run large clinical trials

One other aspect of the Danish study helped achieve the high enrolment rate. What was being done to the participants did not require their informed consent.

The seniors were randomly assigned to receive either a version of a message encouraging them to get the flu vaccine, or no message at all. They were merely given information to help them make a decision.

In a more usual clinical trial, where health and healthcare are affected in an important way (such as which medication they will receive), a person is not enrolled unless they have agreed to participate. It is a much more difficult and expensive trial to conduct,

due to the time and effort of obtaining the consent.

The Denmark team has already moved on to show that their framework can work for even those types of more demanding trials. They are now conducting a trial testing whether a higher dose of flu vaccine is better than the standard dose that is used in Denmark for many older individuals.

To do this, the researchers determined they needed to ask 800,000 people to participate, with at least 200,000 agreeing to enrol. These numbers were smaller than those for the Nudge-Flu trial, but they are still stunningly large in the world of clinical trials and for a country whose entire population is under six million people.

A smaller pilot was successfully conducted with 12,000 people, which suggests they would indeed be able to complete the larger, full-size

study, which is on track to be completed in 2024.

Singapore's conducive environment

The Danish researchers proved that a small country can successfully conduct huge trials on public health issues such as flu vaccination.

Like Denmark, Singapore has several characteristics that could be conducive for running different types of large-scale trials. Singapore has infrastructure in place for the collection and sharing of medical information. It has a world-class community of top researchers who want to do even more cutting-edge research.

And there is a strong level of trust in the government. The 2023 Edelman Trust Barometer found that the government remains the institution most trusted by people in Singapore, ahead of the media, business and non-governmental organisations.



Almost
1 MILLION
Danish citizens
participated in the
Denmark Nudge-
Flu trial in 2022



A centralised email system and country-wide databases could be used to efficiently identify possible research participants.

And obtaining informed consent—often the costliest and most labour-intensive step in a clinical trial—could be done electronically, using those systems. In the wake of the pandemic, there has been a growing recognition that remote consent is perfectly ethical and not inferior to in-person consent.

Myopia and other health problems of special concern

Conducting more home-grown clinical trials has been accurately described as a "win-win for patients and the economy". The companies conducting the trials will be creating new jobs, and if the trials lead to the development of new products, the manufacture of those products in Singapore can synergistically create even more jobs.

Among other things, such local research activity creates the opportunity for trials that will directly advance priorities in Singapore.

Healthier SG is the national initiative to make people healthier by preventing the development of chronic diseases, instead of treating them. But changing behaviour is always challenging, so information from Singapore-designed trials can be vital in attaining those goals.

Similarly, trials can be designed to tackle specific health problems of special concern in Singapore, but less priority elsewhere. Singapore has been described as the "myopia capital of the world", where the condition is "increasing the risk of irreversible blindness in millions of people" and generating annual healthcare costs of more than US\$700 million every year.

Solutions to a problem of this scope will likely require a better understanding of the causes and possible preventive measures. To what extent does providing secondary school children with laptops or tablets worsen the development of myopia, and is that trade-off worth making due to the educational benefits? How should the mix of cultures in Singapore shape anti-myopia measures?

These are Singapore-specific questions, and Singapore-specific research is needed to provide the most meaningful answers.

As we move on from the COVID-19 pandemic, we shouldn't forget that substantial factors in Singapore's successful campaign against the virus were the various ways in which local research—regarding how the virus spread, and how it can be treated and prevented—was rapidly conducted, with the results being used to create policy interventions.

Among many examples, Singapore researchers created and tested a first-in-the-world COVID-19 serology test and multiple Singapore hospitals partnered National Institutes of Health in the US to test remdesivir as a treatment, which played a role in obtaining access to COVID-19 treatments for patients in Singapore. That is a Singapore success story well worth repeating.



Neighbourhood Health Service 2023: Touching Lives, Serving the Underserved

BY NEIGHBOURHOOD HEALTH SERVICE (NHS) PROGRAMME DIRECTORS IVAN LI, MATTHIAS HO, PHASE II NUS MEDICINE STUDENTS AND DR GOH LAY HOON, NHS MENTOR, DEPARTMENT OF FAMILY MEDICINE, NATIONAL UNIVERSITY HEALTH SYSTEM (NUHS)

Mission and history of NHS

The NHS is a population outreach project of the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine). It started in 2007, and is in its 17th year. Since its founding, NHS has been focusing on helping residents from lower socioeconomic backgrounds to access healthcare. Many of these residents are elderly and living in rental flats.

Despite overall healthcare improvement and innovation over the years in Singapore, residents living in rental apartment blocks have remained more vulnerable and disengaged from the healthcare system than the average Singaporean¹. These residents face socio-economic, psychological, knowledge, and cultural barriers that prevent them from accessing healthcare regularly^{2,3}. Moreover, chronic

diseases and their complications remain common; residents from disadvantaged communities are especially at risk due to suboptimal health-seeking behaviours.

Hence, NHS aims to identify residents who have fallen through the cracks, break down barriers to healthcare access, and reconnect them to the healthcare system. In addition, NHS has an ongoing



Minister Desmond Lee taking a selfie with the NHS Committee and NUS Medicine Faculty Members at the NHS Screening on 28 October 2023.

NHS 2023 Screening – All about the residents

We wanted to be a “one-stop shop” for busy residents to be screened for multiple diseases in one visit. Hence the screening modalities included blood taking, functional screening for seniors, cancer screening, social work screening, falls risk assessment, dental health survey and health education. Our partner providers include the National University Health System, Health Promotion Board, Agency for Integrated Care and the Singapore Cancer Society. In addition, students from NUS Social Work and Singapore Institute of Technology Physiotherapy, members from Singapore Physiotherapy Association, and staff from the National University Centre for Oral Health also lent their support to the event. All services were provided free of charge to residents.

On the days of the outreach, student volunteers and committee members accompanied residents through the screening stations. Wheelchairs were also deployed to bring residents with mobility issues to and from their homes and the screening venue.

VintageRadio SG, a not-for-profit enterprise that supplies digital radio services, provided the background music to enliven the atmosphere at the venue. Additionally, our adorable NUS Medicine mascots, Meddy and Neddy moved around the venue to interact with the residents. At the end of the screening, we also gave each resident a gift bag containing beverages, snacks, and household items from various sponsors.

Collaboration, building partnerships, and ensuring continuity of care

NHS comprises healthcare students from NUS and other healthcare institutions. We have medical and nursing students from NUS Yong Loo Lin School of Medicine, social work students from the NUS Faculty of Arts and Social Sciences, medical students from the Lee Kong Chian School of Medicine, and physiotherapy students from the Singapore Institute of Technology. Drawing on each other’s expertise to run the various stations at the NHS screening event, healthcare students were exposed to the benefits of working as a team and how collaboration enables them to serve the community holistically.

An elderly resident accompanied by a volunteer, to have his blood taken at the phlebotomy station during NHS 2023.



research arm. As with previous years, we will be analysing the data gathered from this year’s screening exercise to gain insights into the health status and needs of this year’s screened population.

Outreach by NHS

For 2023, NHS chose to engage with residents in the Boon Lay district because of its high concentration of rental blocks. The screening was conducted on 28 and 29 October at the Boon Lay Community Club. The Minister for National Development, Mr Desmond Lee, together with local grassroots leaders and members from the NUS Medicine Office for Students attended the event.



Concurrently, we brought together various community and healthcare partners to successfully conduct this year's screening event. Besides leveraging our partnership with Boon Lay district, which is part of the Healthy Precinct initiative that aims to integrate health promotion efforts in the community, NHS also actively works with community partners in health promotion, including the Ministry of Health Office for Healthcare Transformation and the NUHS Regional Health System Office.

Additionally, NHS facilitates the referral of Boon Lay residents with newly diagnosed chronic conditions to their GPs or polyclinic doctors. We engaged community partners such as Boon Lay Social Service Office, NTUC Crest, and Thye Hua Kwan Family Service Centre, to ensure continuity of follow-up and care beyond the screening event.

Post-screening plans

NHS has put into place an active follow-up strategy to ensure that residents with newly detected chronic conditions, or previously diagnosed but uncontrolled conditions, take active steps to manage their health. In the months after the screening, NHS will follow up with vulnerable residents from the rental blocks. We will make phone calls to check on the well-being and health status of residents, and also determine whether they have sought further medical attention for their identified problems.



NHS committee member and volunteers knocking on doors in Boon Lay on 14 October 2023 to publicise the NHS Screening.

We will also make home visits for patients with more complex situations such as multi-morbidity or mobility issues. During these visits, we will seek to understand their underlying beliefs and motivations using tools like motivational interviewing. The committee will then connect the residents to the appropriate community resources and assist them in coming up with possible solutions to overcome their challenges in accessing healthcare. As a new initiative this year, we will be partnering our NUS Social Work friends in the follow-up programme, and assisting the residents with their Healthier SG enrolment.

Lastly, NHS aims to raise awareness and educate residents on disease prevention and management, as well as correct misconceptions about health.

We believe that targeted education and sustained engagement will empower residents to take ownership of their health and induce positive health-seeking behavioural changes. Hence, NHS has plans to launch a pilot health education programme under our Publicity, Health Education and Community Outreach Committee this year.

Reflections

NHS has come a long way since 2007. Entering a new district in Boon Lay this year meant building fresh relationships with new partners. This has also afforded us a fresh opportunity to rethink how NHS can evolve alongside other national healthcare programmes and promotion efforts, including the recently launched Healthier SG.

¹ Wee LE, Lim LY, Shen T, Lee EY, Chia YH, Tan AYS, et al. Choice of primary health care source in an urbanized low-income community in Singapore: a mixed-methods study. *Family practice*. 2014;31(1):81-91.

² Wee LE, Cher WQ, Sin D, Li ZC, Koh GC-H. Primary care characteristics and their association with health screening in a low-socioeconomic status public rental-flat population in Singapore- a mixed methods study. *BMC Family Practice*. 2016;17(1):16.

³ Wee LE, Tsang TYY, Yi H, Toh SA, Lee GL, Yee J, et al. Loneliness amongst Low-Socioeconomic Status Elderly Singaporeans and its Association with Perceptions of the Neighbourhood Environment. *International Journal of Environmental Research and Public Health*. 2019;16(6):967.

NUS Nursing Nets Fourth American Academy of Nursing Fellowship

Assistant Professor Shawn Goh is the fourth academic from Alice Lee Centre for Nursing Studies (NUS Nursing), National University of Singapore Yong Loo Lin School of Medicine to be inducted into the American Academy of Nursing (AAN) as a Fellow. The other AAN Fellows are Professor Wang Wenru, Professor He Hong-Gu and Assistant Professor Catherine Dong.

A/Prof Shawn Goh was among one of 253 nurse leaders inducted at the New Fellow Induction Ceremony that took place on 8 October 2023 in Washington DC, US. Retracing his journey from the beginning, he chats with *MediCine* about his passions, his most memorable project, current research focus, and aspirations for the future.

MediCine: Congratulations on your achievement! How did you feel when you first knew that you would be in AAN's 2023 Class of Fellows?

A/Prof Goh: I didn't expect that I would be inducted—so it was a very pleasant surprise. With around 400 fellowship applicants from around the world and only 253 inducted, it is an honour to be the only Fellow from Singapore inducted into this prestigious Fellowship in 2023. Additionally, this year happens to be the 50th anniversary of the AAN. This makes my induction extra special.

MediCine: You attended the induction ceremony. How was it?

A/Prof Goh: Just imagine, the people I met at the ceremony are people who write models we use in our teaching, people we cite in our research papers, and



people whose work influence how we practice as nurses. Then there are also the nurses who sit in the US Senate, influencing policy across the whole US. It's very inspiring to come face-to-face with all these people and see how the Academy actualises its mission of impacting people's lives. But if I were to choose one favourite moment, it has to be when I got to take pictures with my idol, Emerson Ea, whose works I cited in my own PhD thesis.

MediCine: Can you share with us the journey leading up to your AAN fellowship?

A/Prof Goh: I started off in the practice as a mental health

nurse. Although I subsequently moved on to teaching, I never forgot my beginning. Thus, when I pursued my Master in Nursing in 2009, I decided to take the opportunity to do something that can help to advance mental health knowledge and healthcare. During this time, I realised that a lot of our knowledge about mental healthcare came from research and studies conducted overseas. While the literature is useful in providing guidance, differences in cultural and context limit their usefulness and applicability to our situation. That was how I got started on research—and kept going.

↑
A/Prof Goh at the American Academy of Nursing induction ceremony.

Over the years, mental health has seen growing interest. People have become more open to talking about it and are more aware of mental health needs. Correspondingly, there is also a shift in research focus. The emphasis is increasingly changing from studying about reactive care of the disease state to preventive strategy—like how to protect the mental well-being of people like you and me. Insights into these pertinent issues help to inform policymakers, and hopefully come in useful in the future.

One such example is my research on “The Impact of COVID-19 on Nurses Working in a university health system in Singapore: A Qualitative Descriptive Study”. Published at a time when little was known about COVID-19 and vaccines were still under development, the study proved to be timely and useful for subsequent research done during the pandemic. It was the top cited article in the *International Journal of Mental Health* from 2020 to 2021, and again from 2021 to 2022. While this study is unlikely to remain as the top cited paper forever, my hope is that the knowledge can help future nurses and future healthcare workers if another pandemic should happen.

As much as my curiosity and thirst for learning guides my research, they also influence the way I teach my classes. The relationship I have with my students is bi-dimensional. I am simultaneously a teacher and a student—I impart what I know from my practice, reading and research to my students, but I also learn about social media and other trends from

them. This makes teaching very fulfilling and stimulating—some of these interactions gave life to my research topics.

MediCine: What is next on the horizon for you?

A/Prof Goh: I see the fellowship as an affirmation of what I’ve been doing. Hence, I am going to keep doing what I am passionate about—teaching and research. There is a certain synergy between the two. For instance, some of my research involves teaching or the evaluation of my teaching outcomes. Other times, I gained a deeper understanding of

issues patients face through my research on the ground. I share these in classes to better prepare students who are eventually going to be nurses in the field one day.

The blending of teaching and research has brought me much joy over the years—they provide learning opportunities and quench my thirst for knowledge. Of course, not every day is sunshine and rainbows, and there are times when I feel less enthusiastic. But I embrace every aspect of teaching and research, including the challenging ones.



This is the fourth consecutive year that someone from NUS Nursing is inducted as an AAN Fellow. As a fairly young school in a small city state, this is an achievement and a recognition of the work that we do in Asia.”

Dr Shawn Goh, Assistant Professor, NUS Nursing



About the American Academy of Nursing Fellowship

With over 3,000 Fellows, the American Academy of Nursing fellowship comprises Nursing’s most accomplished leaders in education, management, practice, and research. More than a recognition of one’s achievements within the Nursing profession, each Academy Fellow has the responsibility to contribute their time and energy to six areas.

- Enhance quality of health and nursing
- Promote healthy ageing and human development across the life continuum
- Reduce health disparities and inequalities
- Shape healthy behaviours and environments
- Integrate mental and physical health
- Strengthen the nursing and health delivery system, nationally and internationally

Winning Hearts and Minds: Multidisciplinary Team Probes Mysteries of Cardiocerebral Diseases

BY DR SIA CHING HUI, CONSULTANT, DEPARTMENT OF CARDIOLOGY, NATIONAL UNIVERSITY HEART CENTRE, SINGAPORE AND JUNIOR ACADEMIC FELLOW, DEPARTMENT OF MEDICINE, NUS YONG LOO LIN SCHOOL OF MEDICINE

Up to a fifth of stroke patients do not present with a history or cause. We still do not know what the optimum treatment duration for a patient with a blood clot in the heart is. Patients experience a loss of memory and mood after a heart attack and have worse outcomes, but we do not know exactly why nor how to prevent it. This realisation of a pressing need has been the catalyst for our investigation into the complex interplay of cardiovascular and neurological diseases.

Both systems are linked by shared risk factors of disease, common pathophysiological mechanisms, and the extensive crosstalk between the heart and the brain. To delve deeper into this field, we created an interdisciplinary research team, StroCar, in 2019. This marked the beginning of an ambitious journey to unravel the intricacies of

the linkages between heart and brain diseases—one of the most formidable challenges in contemporary healthcare.

The burden of cardiocerebral diseases

The urgency of this quest is underscored by alarming statistics. In Singapore, ischaemic heart disease and cerebrovascular diseases were responsible for nearly a quarter of all deaths in 2021.





Globally, cardiovascular disease, neurological disorders and mental health issues collectively account for 616 million disability-adjusted life years. This staggering figure reflects not just mortality, but a profound loss of healthy, productive life years. Confronting this stark reality, StroCar aims to alter the trajectory of these diseases, reducing both morbidity and mortality.

The StroCar initiative: A multidisciplinary approach

Led by Dr Sia Ching Hui from Cardiology and Drs Leonard Yeo and Benjamin Tan from Neurology, the team embodies a synergy of diverse expertise. This collaborative environment fosters a dynamic exchange of ideas, transforming everyday clinical challenges into opportunities for research and discovery. Active discussions of clinical conundrums faced in daily practice serve as inspiration for our research. We actively

collaborate across a range of specialties, including Neurosurgery, Neuroscience, Psychiatry, Psychology, Endocrinology, Hepatology and Emergency Medicine. We also collaborate with centres in the United States, United Kingdom, Europe and Asia. In addition, one of the team's core missions is to train the next generation of clinical investigators—the team is continuously enriched by an influx of residents and medical students, ensuring the perpetuation of knowledge.

Research focus and methodologies

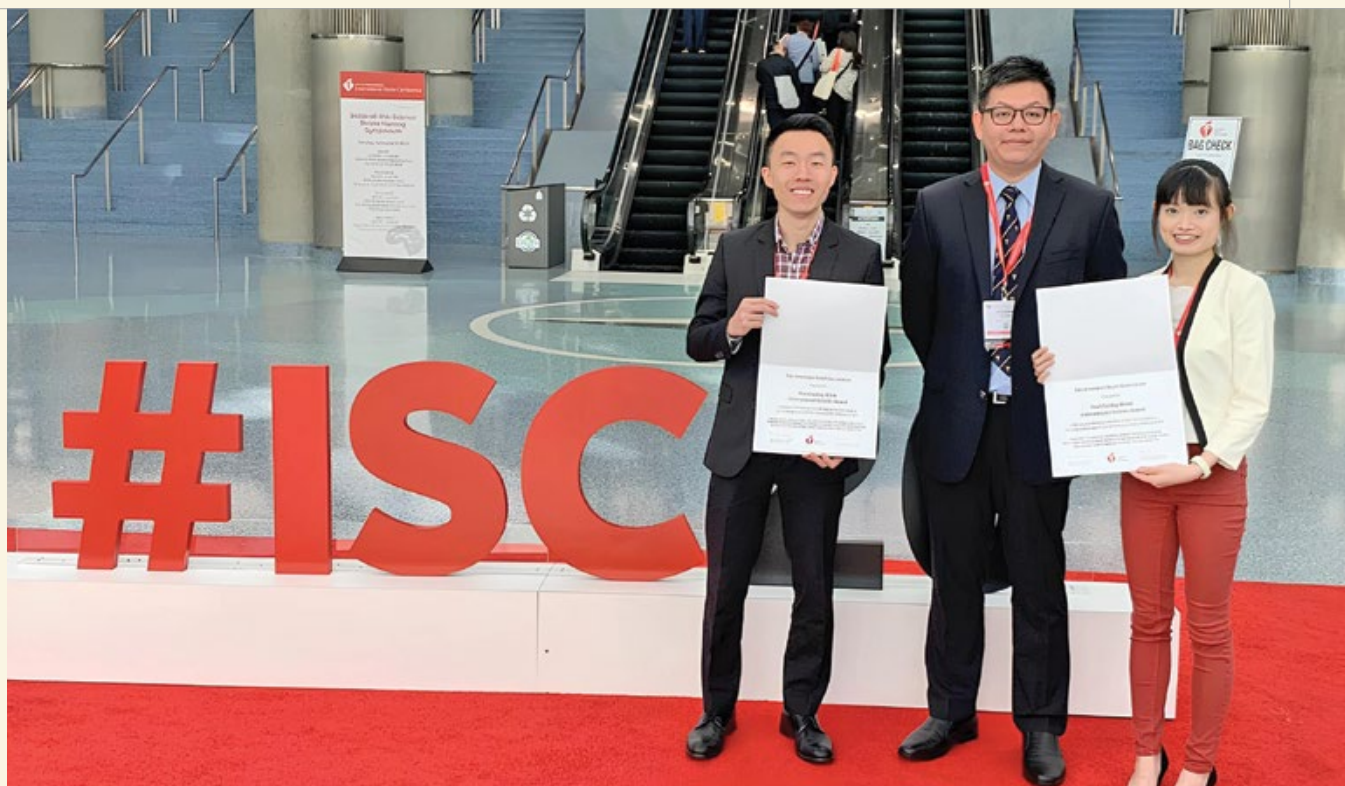
StroCar's research spans a wide spectrum, investigating conditions like left ventricular thrombosis, cardio-cerebral infarction, embolic stroke of undetermined source (ESUS) and cardio-cognitive disease. Methodologically, the team employs a blend of retrospective and prospective cohort studies, meta-analyses, and advanced novel imaging and deep-phenotyping techniques.

This multifaceted approach allows for a comprehensive understanding of disease pathogenesis and progression.

Significant strides have been made by team members. Dr Sia Ching Hui's exploration into cerebral dysfunction post-myocardial infarction is supported by the National Medical Research Council's



Globally, cardiovascular disease, neurological disorders and mental health issues collectively account for 616 million disability-adjusted life years. This staggering figure reflects not just mortality, but a profound loss of healthy, productive life years. Confronting this stark reality, StroCar aims to alter the trajectory of these diseases, reducing both morbidity and mortality.”



↑
 Left:
 Dr Sia Ching Hui (first from left in front row) and Dr Benjamin Tan (second from left in back row) with internal medicine residents from NUHS who are part of the StroCar team.

Right:
 (From left to right) Dr Aloysius Leow, Dr Benjamin Tan, and Dr Jamie Ho at the International Stroke Conference, with the Paul Dudley White International Scholar Awards.

(NMRC) New Investigator Grant and Transition Award. Dr Benjamin Tan integrates genomics and neurovascular imaging to unravel precise mechanisms, and functional outcomes and recovery in young adults with stroke. He is supported by both intramural and extramural fellowships. Dr Leonard Yeo's study into intracranial stenosis and stroke biomarkers is also supported by NMRC. We are also leading a cutting-edge programme in studying patients with embolic stroke of undetermined source, using a novel hybrid cardiac positron-emission tomography-magnetic resonance imaging scan to study the pathogenesis of ESUS.

Recognition and achievements

The team's mentorship programme includes Drs Aloysius Leow and Jamie Ho, both internal medicine residents at the National University Health System

(NUHS). They have garnered international acclaim with Young Investigator Awards and the Paul Dudley White International Scholar Awards, reflecting the relevance and quality of StroCar's research. Dr Teo Yao Hao, also an internal medicine resident at NUHS, is the recipient of the selective Dean's Fellow award at NUS. Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) students mentored by StroCar have also won various awards at the school and international level. Mr Teo Yao Neng, currently a phase 5 student, was the abstract winner for the previous joint American College of Cardiology/ Singapore Cardiac Society Meeting. These accolades are validations of the team's work.

Vision for the future

Looking ahead, StroCar aspires to broaden our horizons. Expanding the core team, forging global collaborations, and enhancing

patient education and advocacy are pivotal to our future endeavours. The team actively seeks like-minded individuals and institutions to join this pioneering journey. StroCar's website (www.strocarcollab.com) showcases our achievements and invites participation from those inspired by our mission.

Conclusion

StroCar is not just a clinical or research initiative. We aspire for StroCar be a beacon of hope in the fight against cardiocerebral diseases. The multidisciplinary approach, combined with a commitment to innovation and education, positions StroCar uniquely to address some of the most pressing medical challenges of our time. As the team continues to unravel the complexities of heart-brain interactions, we aim to make discoveries that could transform medical practice and improve countless lives.

The Road Less Travelled – Splicing in Trans: From a Natural Phenomenon to Gene Therapeutic Applications

BY DR VOLKER PATZEL, DEPARTMENT OF MICROBIOLOGY, HEALTHY LONGEVITY TRANSLATIONAL RESEARCH PROGRAMME, YONG LOO LIN SCHOOL OF MEDICINE, NATIONAL UNIVERSITY OF SINGAPORE

One year after the discovery of *cis*-splicing by the teams of Roberts and Sharp^{1,2}, Walther Gilbert suggested that the combination of different exons of a single gene could lead to the generation of various mRNA isoforms³, a process that is today known as *alternative splicing*. Constitutive and alternative splicing isn't mutually exclusive, which solves the former problem that for a continuous evolutionary process, essential genes don't need to duplicate before one version can mutate to evolve new gene functions.

Alternative splicing generates new functions by creating new exons within existing genes and can suspend the negative selection pressure against evolutionary changes of functional genes. Thus, alternative splicing opens nearly neutral paths for evolutionary changes. Alternative splicing represents a key mechanism that is recruited by most DNA viruses, and nuclear-replicating RNA viruses to generate the full repertoire of protein functions⁴. RNA *trans*-splicing represents a special form of alternative splicing in which sequences of distinct precursor pre-mRNA transcripts are joined *in trans*.

In the mid-90s, first experimental evidence was obtained showing that mammalian cells can combine natural pre-mRNAs to form new mRNA via RNA *trans*-splicing^{5,6}. *Trans*-splicing in mammalian cells differs from small leader RNA (SL RNA) *trans*-splicing reported earlier in trypanosomes and *caenorhabditis elegans*, is independent of SL RNA, and mediated by the spliceosome of the cell. Computational analyses of cDNAs from a gene databank indicated one percent of all sequenced mRNAs to be chimeric⁷, some of which might be synthesised by RNA *trans*-splicing. Up to date,

several examples of naturally occurring mammalian RNA *trans*-splicing have been reported, many of them involving viral transcripts⁸⁻¹⁴. For many viruses, economy in genome size represents a common theme, and generating new protein functions by combining RNAs via splicing in *trans* does not require a genome enlargement. Our finding that the SV40 virus uses homologous RNA *trans*-splicing to generate a functional protein, namely a highly transforming 100 kD super T antigen, supports this hypothesis and demonstrates that viruses engage the mechanism of RNA *trans*-splicing to maximise their transcriptomes and proteomes¹⁵. SV40 RNA *trans*-splicing was found to be highly

efficient with 50% or more viral transcripts being involved in the *trans*-splice reaction. The knowledge and understanding of the mechanism of RNA *trans*-splicing not only points towards a role of RNA *trans*-splicing in the generation of novel viral gene products, but also offers promising perspectives for various applications.

Trans-splicing based repair of gene expression

If a gene is functionally impaired by mutagenesis, gene complementation therapy may be explored to restore the defect function. Therefore, complete functional genes are delivered into target cells using viral or non-viral vectors. Many of these vectors experience cargo size limitations. If the gene

complementation approach is successful, both the defect and the recombinant genes are being expressed and eventually compete for cellular functions. Sometimes, mutated genes express harmful or carcinogenic proteins.

Then, a functional gene knockdown e.g. using RNA interference is indicated which leads to the partial loss of the respective gene function. RNA *trans*-splicing enables repair of defect gene functions, i.e. replacement of defect with intact gene functions on the level of the pre-mRNA, thereby combining the advantages but avoiding the disadvantages of the two approaches discussed above. For applications, *trans*-splicing RNA (tsRNA)

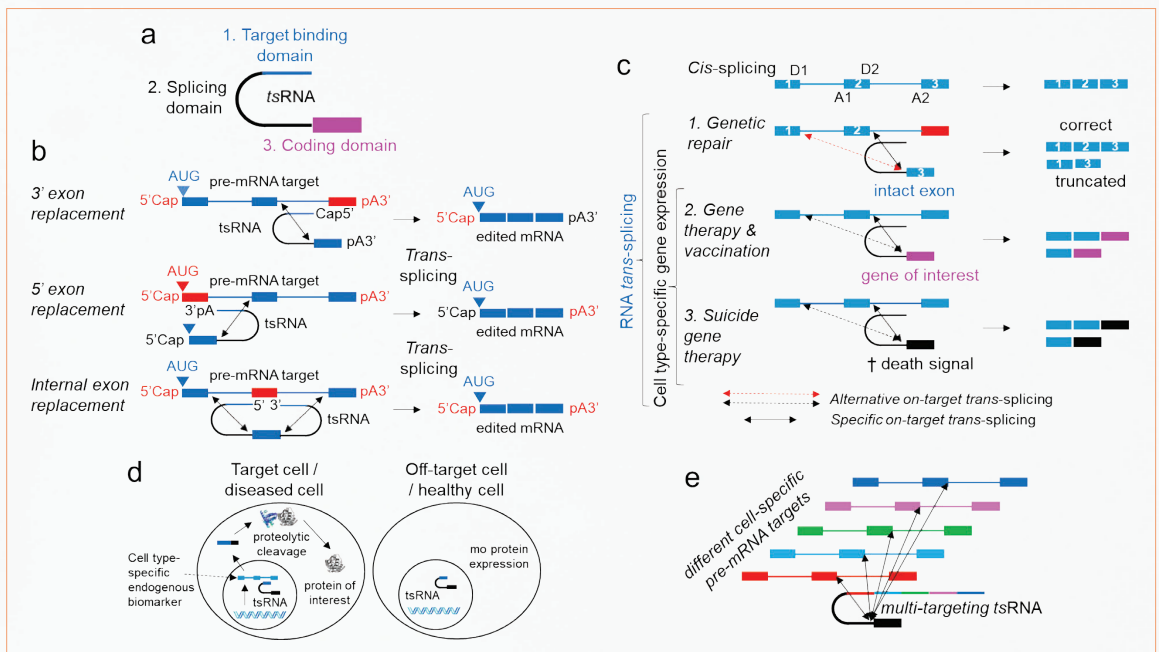
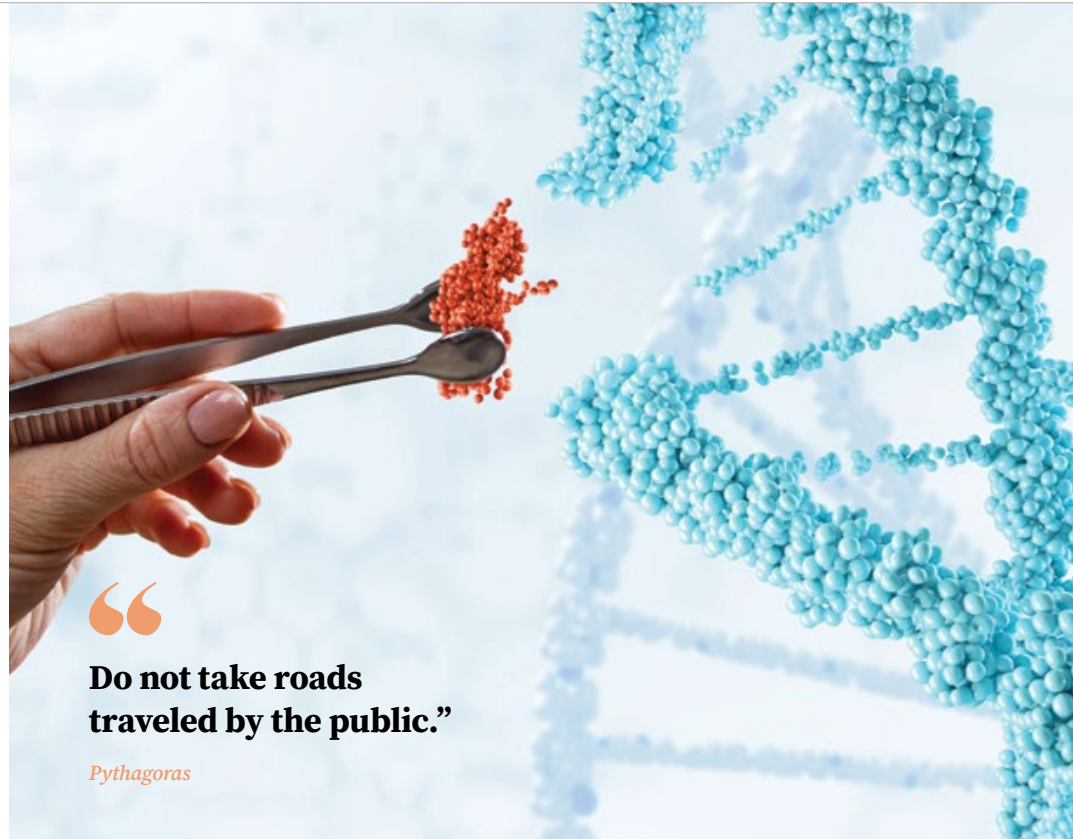


Figure. a, Design of a *trans*-splicing RNA (tsRNA), using the example of a tsRNA for 3' exon replacement. b, RNA *trans*-splicing mediated genetic repair via 3', 5', and internal exon replacement. c, *Trans*-splicing based genetic repair strategies suffer from alternative on-target *trans*-splicing; strategies based on cell type-specific gene expression benefit from alternative on-target *trans*-splicing. d, *Trans*-splicing triggers gene expression selectively in target/diseased cells but not in off-target/healthy cells. Initially formed chimeric proteins can efficiently be cleaved via proteolytic cleavage. e, Design of *trans*-splicing RNA comprising multiple target binding domains.

is designed to comprise three functional domains: a domain coding for the protein or polypeptide to be fused to the targeted gene product, a splicing domain harbouring all sequences required to recruit the spliceosome, and a binding domain (BD) (Figure a). The BD is an antisense sequence that enables the tsRNA to specifically identify the intended pre-mRNA target in the nucleus of the target cell. Once the tsRNA is bound to the pre-mRNA to edit, *trans*-splicing between the two RNAs occurs, triggering the generation of an edited mRNA and expression of an edited protein. *Trans*-splicing RNA can be designed to replace 5' terminal, internal or 3' terminal exons within a pre-mRNA target whereby the target RNA remains in its natural regulatory context (Figure b).

Opposed to RNA editing which is suitable to edit single point mutations within a pre-mRNA, *trans*-splicing based repair can be a more mutation agnostic approach as complete exons can be replaced. The fact that only exons but not complete genes need to be delivered to restore gene function, qualifies the *trans*-splicing technology to be deliverable using any vector technology, including those with apparent cargo size limitations. When compared with the CRISPR/Cas genome editing technology, RNA *trans*-splicing is conceptually much safer as it does not target the genomic DNA. Attempts to develop RNA *trans*-splicing based genetic repair therapies however have faced challenges related to achieving high on-target activity and specificity. RNA *trans*-splicing is competing with *cis*-splicing, the latter of which is favoured as it appears to be an intramolecular reaction



Do not take roads traveled by the public.”

Pythagoras

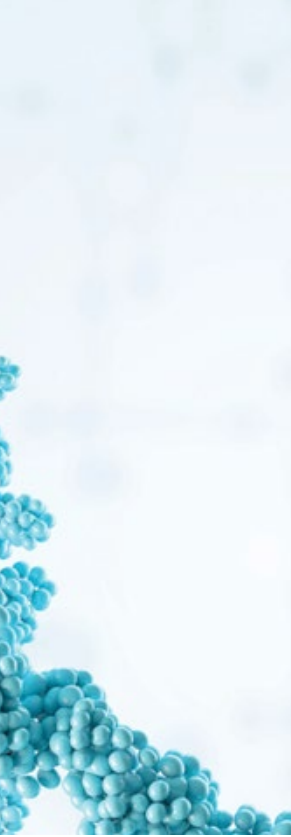
that, unlike *trans*-splicing, does not require two RNAs to find each other in the nucleus of the cell. Another issue is alternative on-target *trans*-splicing, i.e. the fact that a *trans*-splicing RNA might not exclusively splice towards the intended target splice site, but in addition can also approach strong alternative splice sites leading to imprecise editing and the expression of truncated proteins (Figure c). Our studies revealed that alternative on-target *trans*-splicing can be 100-fold more abundant than specific on-target *trans*-splicing¹⁶.

Cell type-specific gene expression

Because of the issues associated with *trans*-splicing based genetic repair, we decided to take a different path. Unlike other research teams and companies in the past, we strategised on using RNA *trans*-splicing to achieve cell type specificity of gene expression.

Cell type specificity is a basic requirement for most gene therapy approaches as it strongly helps to reduce side effects.

Usually, it can be achieved with limited success through targeted delivery and by employing cell type-specific promoters. Intriguingly, RNA *trans*-splicing enables cell type-specific activation of gene expression based on the cell's endogenous pre-mRNA biomarker profile. Therefore, the coding domain of a tsRNA can comprise the sequence coding for any gene of interest and the binding domain is designed to approach a pre-mRNA that is exclusively or predominantly expressed in the intended target cell type(s) (Figure c). Consequently, into whatever cell such a vector is being delivered, protein expression will only be triggered in target cells expressing a selected cell-specific pre-mRNA.



Resulting chimeric proteins can efficiently be cleaved via proteolytic cleavage to produce the protein of interest (Figure d). Such pre-mRNA targets have been described or can virtually be found for any target cell of interest. For many target cells, even multiple unique or overexpressed pre-mRNAs have been reported. We first designed tsRNA featured with multiple BDs each suitable to bind towards one out of a group of selected pre-mRNA targets. This design increased the *trans*-splicing activity 100 to 1,000 folds as it significantly increases the pre-mRNA target concentration (Figure e). In contrast to *trans*-splicing based genetic repair strategies, approaches to employ RNA *trans*-splicing for cell type-specific gene expression are not jeopardised by alternative on-target *trans*-splicing. On the contrary, alternative on-target *trans*-splicing can

even amplify the level of cell type-specific expression (Figure c). For genetic repair or sustained cell specific gene expression, the tsRNA must constantly be available in the cellular nucleus which can only be achieved by a stably expressing integrating vector or the repeated delivery of a transient genetic vector.

Breaking new ground

To evade the above-mentioned delivery issues, we focused on applications that do not require sustained nuclear availability of the tsRNA. These applications include but are not limited to suicide gene therapy, whereby the expression of a death signal is specifically triggered in diseased cells, e.g. tumour or irreversibly virus-transduced cells, with the intention to kill the same without compromising healthy cells (Figure c,d)¹⁶.

Another application can be genetic vaccination. By using RNA *trans*-splicing, antigen expression can selectively be triggered in distinct immune cells to manipulate immune responses. We are currently investigating the suicide gene therapy and vaccination approaches in pre-clinical animal studies. In conclusion, the potential of the RNA *trans*-splicing technology is comparable with that of other groundbreaking RNA technologies. However, its most obvious applications and the most frequently travelled roads are not necessarily those leading to quick success. With an advanced tsRNA design and a focus on the most promising applications, RNA *trans*-splicing is expected to evolve into a valuable technology for gene therapeutic applications.

- ¹ Berget, S. M. & Sharp, P. A. A spliced sequence at the 5'-terminus of adenovirus late mRNA. *Brookhaven Symp. Biol.* 29, 332-344 (1977).
- ² Chow, L. T., Gelinias, R. E., Broker, T. R. & Roberts, R. J. An amazing sequence arrangement at the 5' ends of adenovirus 2 messenger RNA. *Cell* 12, 1-8 (1977).
- ³ Gilbert, W. Why genes in pieces? *Nature* 271, 501 (1978).
- ⁴ Hegel R. HERNANDEZ-LOPEZ and Sheila V. GRAHAM1. Alternative splicing in human tumour viruses: a therapeutic target? *Biochem. J.* (2012) 445, 145-156.
- ⁵ Eul J, Graessmann M, Graessmann A. Experimental evidence for RNA trans-splicing in mammalian cells. *EMBO J* 1995; 14:3226-35.
- ⁶ Eul J, Graessmann M, Graessmann A. In vitro synthesized SV40 cRNA is trans-spliced after microinjection into the nuclei of mammalian cells. *FEBS Lett* 1996; 394:227-32.
- ⁷ Romani A, Guerra E, Trerotola M, Alberti S. Detection and analysis of spliced chimeric RNAs in sequence databanks. *Nucleic Acids Res.* 31, e17
- ⁸ Caudevilla C, Serra D, Miliar A, Codony S, Asins G, Bach M, et al. Natural trans-splicing in carnitin octanoyltransferase pre-mRNAs in rat liver. *Proc Natl Acad Sci USA* 1998; 95:12185-90.
- ⁹ Caudevilla C, Codony C, Serra D, Plasencia G, Roman R, Graessmann A. Localization of an exonic splicing enhancer responsible for mammalian natural trans-splicing. *Nucleic Acids Res* 2001; 29:3108-15.
- ¹⁰ Flouriot G, Brand H, Seraphin B, Gannon F. Natural trans-spliced mRNAs are generated from the human estrogen receptor (hER) gene. *J Biol Chem* 2002; 277:26244-51.
- ¹¹ Kikumori T, Cote GJ, Gagel RF. Naturally occurring heterologous trans-splicing of adenovirus RNA with host cellular transcripts during infection. *FEBS Lett* 2002; 522:41-6.
- ¹² Jehan Z, Vallinayagam S, Tiwari S, Pradhan S, Singh L, Suresh A. Novel noncoding RNA from human Y distal heterochromatic block (Yq12) generates testis-specific chimeric CDC2L2. *Genome Res* 2007; 17:423-40.
- ¹³ Brooks YS, Wang G, Yang Z, Smith KK, Bieberich E, Ko L. Functional pre-mRNA trans-splicing of coactivator CoAA and corepressor RBM4 during stem/progenitor cell differentiation. *J Biol Chem* 2009; 284:18033-46.
- ¹⁴ Desai MM, Tumurbataar S, Zhang Y, Chan LN, Sun J, Chan TS. 2011. Aberrant transcription and post-transcriptional processing of hepatitis C virus non-structural genes in transgenic mice. *Transgenic Res.* 20:1273-1284.
- ¹⁵ Eul J, Patzel V (2013). Homologous SV40 RNA trans-splicing: a new mechanism for diversification of viral genotypes and phenotypes. *RNA Biology* 10:11, 1-11, 2013.
- ¹⁶ Poddar S, Loh PS, Ooi ZH, Osman F, Eul J, Patzel V. RNA structure design improves activity and specificity of trans-splicing triggered cell death in a suicide gene therapy approach. *Molecular Therapy: Nucleic Acids* 11, 41-56, 2018.

Part 2

What the Living Can Learn from the Dying (and Their Families)

BY DR NOREEN CHAN, SENIOR CONSULTANT AND HEAD, DIVISION OF PALLIATIVE MEDICINE, NATIONAL UNIVERSITY CANCER INSTITUTE, SINGAPORE

Some years ago, I had written an article about how caring for dying patients and families had taught me so much that cannot be found in textbooks.

It was only possible to give a few examples to illustrate that the work we do in Palliative care is both art and science, and while it can be challenging work, it is also immensely rewarding. Not just the chance to witness the rich tapestry of the human condition, but to develop a healthy respect for the mystery of our existence, how not everything can be explained (nor needs to be).

And so, let me share a few more stories about patients whom I have been privileged to care for, and the lessons imparted:

Is it a wish, or is it a goal?

Twenty years ago, when I was based at Dover Park Hospice, a man was admitted with paralysis from cancer that had invaded his spine. He could only sit up upright for brief periods because his spine was too unstable to support his torso, so he spent most of his time in bed or in a reclining wheelchair. One day at the team meeting, his case was brought up for discussion because the staff were concerned about his ability to cope with his illness. “He keeps talking about going on a cruise next year” ... “he told me he would soon go ballroom dancing again” ... yet we all knew he would not

live longer than a few months. “He’s in denial!” was the team’s consensus.

So, I sat with him and we talked; mostly he talked and I listened, about his life before cancer, what he had enjoyed doing, what he still hoped to do. He had been saving for a trip to Machu Picchu, and had done a lot of reading and research about it. I responded with “Wow that sounds amazing, a dream holiday...” and he broke in with, “I think maybe it will just be a dream...” and became pensive. Subsequently I learnt that he knew exactly what was going on with his body, and his talking about these so-called



unrealistic plans was just wishful thinking aloud. What he wanted from us was to acknowledge his right to have big dreams and grand plans, even if they were not going to come true.

He taught me that we must know the difference between a wish and a goal. That it is alright to dream. And that denial is sometimes a defense mechanism so we can wake up in the morning and face the day.

It's not so much the days in your life, as the life in your days

Mr Lee could not speak as a result of his cancer, but he had no problem communicating and connecting with others. He arrived at my clinic for the first time with a pre-written note about his thoughts on palliative care and what he considered to be quality of life, which for him meant a degree of independence and being able to indulge in his hobbies, especially Chinese painting and calligraphy. I had referred him to HCA Hospice Care so that he could be supported at home, and they helped him to arrange an exhibition of his work.

D was a 19-year-old young man with a brain cancer which had affected his speech and ability to walk. Yet his dream was to finish his 'A' Levels, especially English and Mathematics which were his favourite subjects. It was questionable if he could take even one subject, let alone two, but it did not stop the medical team and his school from trying to get him closer to his goal, even if it meant him taking the examination in hospital

or at home, with an individual invigilator and extra time to accommodate his disabilities.

It is easy to forget that people with life-limiting illness still wish to experience the richness of life. An older person might be delighted by a celebration of a life well lived, such as an exhibition, photo diary, recipe book etc. But for a young person, a different approach might be needed, for example working towards important milestones of growing up (graduation, National Service etc.). It might not be possible to reach the destination, but the journey still matters.

Being grateful for the little things

J was 23 years old and had been in hospital for a few months, but his aggressive leukaemia was not responding to treatment. He was a big Transformers fan and was hoping to live long enough to watch the latest film when it was released. Due to complications of his disease, he was confined to bed most of the time. When the Haematology team learnt of this, they managed to arrange for a special screening of the film, as well as an outing to Resorts World Sentosa to experience the newly opened Transformers Ride.



12/2/2020.

Palliative Care

Palliative care is a specialised approach to care for people with serious illnesses. To improve the quality of life of patients and families.

My present needs:

- Some family care helper to assist some daily treatment.
- Regular post-treatment from
- Quality of life - I'm quite happy with my hobby on Chinese Calligraphy & painting with some gardening.



Top: Image of Mr Lee How Son, taken from HCA Hospice's Instagram page, 5 December 2020.

Bottom: Mr Lee How Son's notes.

It was a major logistic exercise because J needed medical and nursing escorts, ambulance, wheelchair etc., but the ward staff put together a team of volunteers to accompany him throughout (with tickets to RWS sponsored by the senior doctors). You might have thought that the exciting lineup of events at Sentosa would be the highlight of his day, but when he was pushed out of the hospital to the ambulance, he looked up from his stretcher, beamed and said excitedly “I can see the sky!”.

J did not have immediate family, only an elderly aunt, so the hospital ward was his home and the ward staff his family. Despite his difficult circumstances he remained upbeat, open and generous. His farewell message on his Facebook page and to the ward was “Try to stay happy. There’ll be cloudy days, but one day the sun will come out. Just like the time I had here”.

Sometimes you are exactly who and where you need to be

Another story from my time at Dover Park Hospice: One night, I had come back to the hospice on call, and while I was seated at the nurses’ station writing up my notes, a young man approached me from one of the rooms opposite. I guessed that he was a relative keeping vigil because those rooms were reserved for dying patients.

He asked how we know when someone is going to take his last breath. I told him some basic information but also asked him why he was asking. He explained that it was his father who was dying, and as he was the only child, his aunts and uncles had instructed that at the



It is ironic, then, that acknowledging death may actually help us to have a more fulfilling life. If nothing else, it can help us prioritise how we want to live well, before leaving well.”



last breath, he had to kneel and call his father’s name. He had been camping at the bedside day and night wondering when the moment would come.

I told him we never really know when the exact moment will be, but since I was already there, I offered to do a quick check just to make sure his father was comfortable. As I was doing my examination, I suddenly noticed out of the corner of my eye that the patient’s breathing was starting to change. “Oh, I think it is happening” I said, and together, we stood and watched over the next few minutes as the breathing slowed and then stopped. I looked at the young man “that was his last breath, he’s passed on” and after the briefest of pauses, he dropped to his knees, called out “Ah Pa” and began to weep.

To this day, I wonder at the chain of events that needed to happen to bring me to the bedside of this dying man, so that his son did not have to be alone. The experience taught

me that the universe does work in mysterious ways, and you will never know when and how you can be of service to another, except to be open to the possibility.

Finally

The knowledge that we will not live forever, the acknowledgement of finitude as part of the human condition, has contributed much to the arts, religion and philosophy. It also affects how we approach our own existence, if we actually stop to think about it. Realistically though, most times we do not, and just carry on as if life will always be this way. Paulo Coelho, in his book “Like the Flowing River”, writes about the contradiction of people—“They live as if they will never die, and die as if they have never lived”.

It is ironic, then, that acknowledging death may actually help us to have a more fulfilling life. If nothing else, it can help us prioritise how we want to live well, before leaving well.

To Bless the Space Between Us

By John O'Donohue

For Death

From the moment you were born,
Your death has walked beside you.
Though it seldom shows its face,
You still feel its empty touch
When fear invades your life,
Or what you love is lost
Or inner damage is incurred.

Yet when destiny draws you
Into these spaces of poverty
And your heart stays generous
Until some door opens into the light,
You are quietly befriending your death;
So that you will have no need to fear
When your time comes to turn and leave.

That the silent presence of your death
Would call your life to attention
Wake you up to how scarce your time is
And to the urgency to become free
And equal to the call of your destiny.

That you would gather yourself
And decide carefully
How you now can live
The life you would love
To look back on
From your deathbed.

Looking for the Right Stuff – The NUS Medicine Admissions Exercise



Each year, the Yong Loo Lin School of Medicine receives applications from aspiring candidates seeking places in its five-year MBBS undergraduate degree programme.

The young men and women who meet the initial qualifying academic requirements are invited to interviews, where they are put through their paces via a series of assessments, including a written exercise. These are designed to probe and ascertain candidates' attitudes and aptitude—while intellectual capabilities are fundamental requirements, qualities such as respect, integrity, compassion, humility, and a commitment to society's welfare are also vital and essential for a career in Medicine.

The search for tomorrow's doctors

At the core of NUS Medicine's admissions process is a group of dedicated faculty and administrators who are entrusted with organising the selection of students with the values that align with those of the Yong Loo Lin School of

Medicine, and which provide the foundation for a career of service in healthcare.

"We look beyond grades to discover those qualities that make outstanding healthcare professionals. While academic prowess is important, personal qualities and values are what the admissions process tries to identify in our candidates," said Associate Professor Marion Aw, the School's Vice-Dean for Students. She leads the NUS Medicine Admissions Team in laying the groundwork for the School's annual selection exercise, an annual event that is months in the preparation.

While candidates who qualify for admissions approach the NUS Medicine selection process with a mix of eager anticipation, excitement and anxiety, the School takes pains to ensure an inclusive environment that is beneficial for students' development.

There are accessibility options for students with different learning needs such as dyslexia, colour deficiency, physical disability and others. Applicants are encouraged to declare their learning needs so that support can be rendered early to cope with the rigours of medical school, A/Prof Aw said.

In addition to 'A' Levels holders, the School also welcomes applications from polytechnic graduates and runs the NUS Medicine Engagement Programme to introduce students from polytechnics and junior colleges to a career in Medicine. Schools are also invited to nominate students who they think are suitable, but who may not have considered Medicine as a possible career.

The programme consists of a non-residential camp and a three- to four-month long mentorship component, and which assigns students to practising clinicians. The students shadow these clinicians and learn about life as a doctor. Financial support is provided by NUS Medicine for participants on financial aid.



Making the list: The interview process

The interview stage of the NUS Medicine admission exercise holds profound significance. Together, the Situational Judgement Test (SJT) and Focussed Skills Assessment (FSA), provide selectors with a good understanding of the strengths, values and likely suitability of candidates for medical studies.

The FSA delves into applicants' attitudes and aptitudes, evaluating skills essential for medical practice. This multifaceted assessment examines attributes such as critical thinking, communication, empathy and problem-solving.

Complementing this, the SJT gauges ethical and situational reasoning. It presents real-world scenarios, where candidates' choices express and demonstrate their views, values as well as decision-making ability.

The School's admissions exercise seeks to gauge attributes beyond knowledge—qualities such as compassion, integrity and adaptability. They provide a platform for candidates to demonstrate their potential as future doctors.

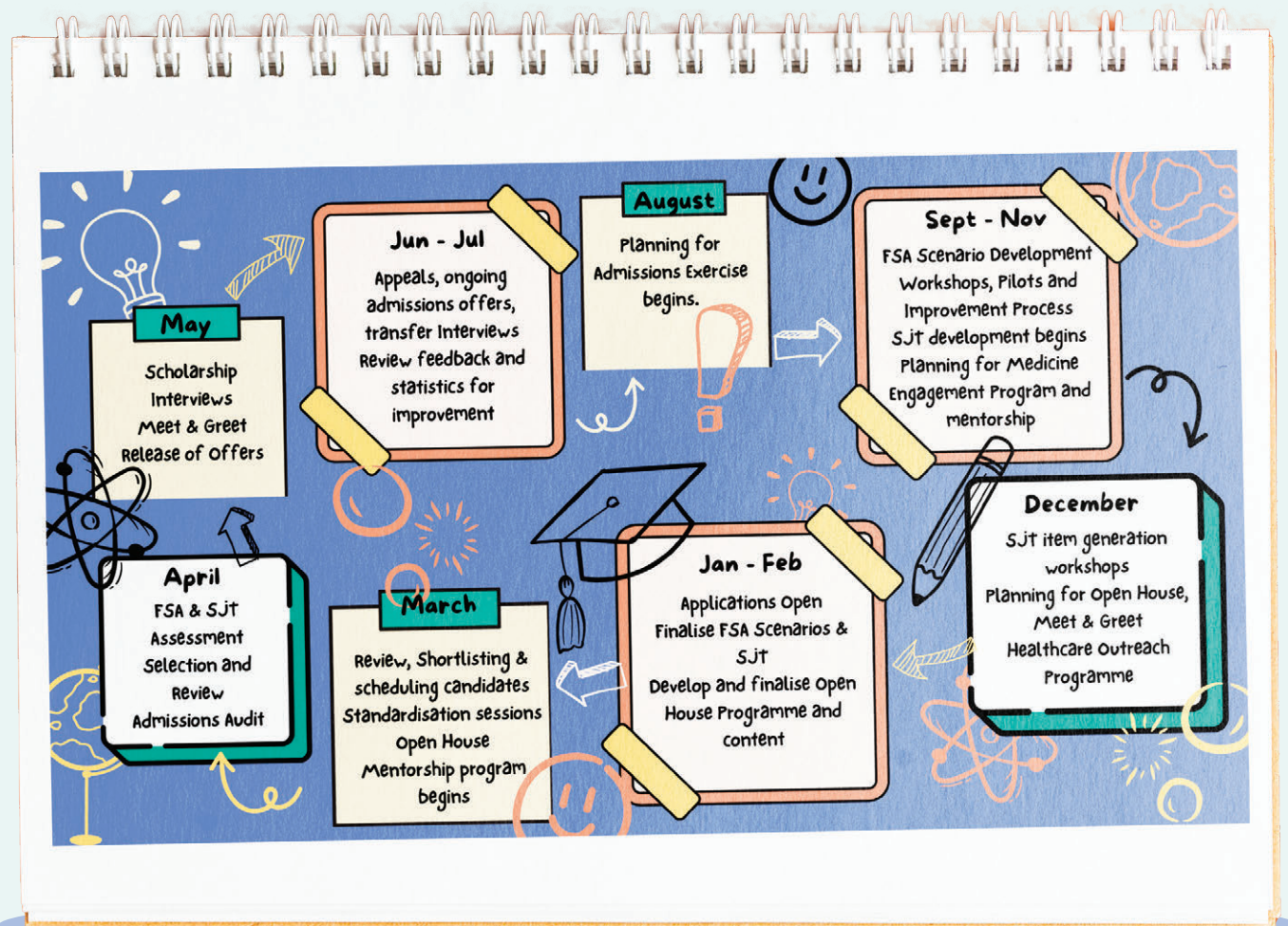
Planning and preparation

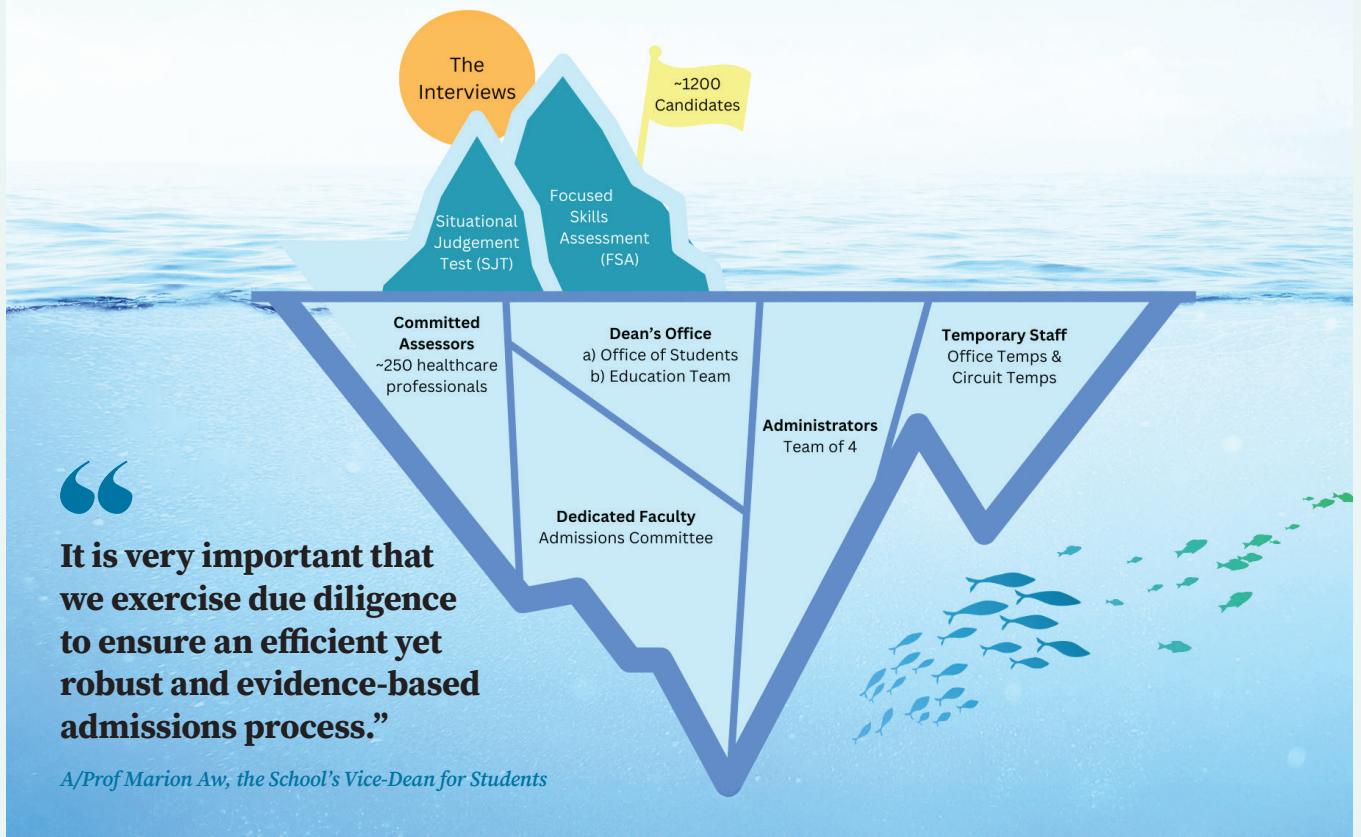
Organising the annual admissions assessment exercise is a continuous process that begins, ends and begins again

with every intake of medical students. Spread across seven days, the admissions assessment accommodates over 1,000 candidates, who have to navigate a written assessment (SJT) and a rigorous six-station FSA. A dedicated team of approximately 250 faculty assessors contribute their time and expertise towards this intricate selection procedure.

For candidates, the day that they spend undergoing selection is for many a culmination of years of hard work, noted A/Prof Aw. "It is very important that we exercise due diligence to ensure an efficient yet robust and evidence-based admissions process," she added.

Contrary to common belief that admissions activities happen only between February and May, the Admissions Team and committee work throughout the year. The Admissions Team starts planning for each upcoming admissions cycle from August of each academic year.





It is very important that we exercise due diligence to ensure an efficient yet robust and evidence-based admissions process.”

A/Prof Marion Aw, the School's Vice-Dean for Students

As one admissions exercise ends, planning for the next one begins

Behind the scenes, NUS Medicine's selection process is guided by the institution's mission and the broader healthcare needs of Singapore. The decisions made extend beyond individual achievements to encompass the collective potential of each cohort, reflecting the School's dedication to shaping the future of healthcare.

For the aspiring doctors who have secured admission, the journey is just beginning. Orientation programmes, mentorship initiatives, and resources are designed to ensure a seamless transition into the life of a medical student at NUS. Campus life offers a plethora of student activities, balancing academic rigour with a vibrant culture. In addition, the network

of the School's 10 Houses enables new students to form strong bonds with their seniors and peers. Very often, these ties endure and last for life, as students graduate and embark on their individual careers as medical practitioners.

Meanwhile, the Admissions Team goes back to work, analysing feedback, improving the existing admissions exercise framework. Quietly but surely and with certainty, the Admissions Office team responsible for the process by which Singapore's future doctors are identified and admitted is going about their work to help shape the future of Medicine.

Conclusion

The path to NUS Medicine is a journey of dedication, determination, and discovery. Understanding the intricacies of NUS Medicine admissions

unveils a world where values align with aspirations, diversity shapes excellence, and holistic healthcare is the ultimate goal. As aspiring medical students set forth on this transformative journey, armed with insights into the heart of NUS Medicine's admissions process, they can stride confidently towards their dreams, knowing that the path they tread is illuminated by NUS Medicine's unwavering commitment to producing compassionate, competent, and impactful healthcare leaders. The Admissions Team at NUS Medicine would also like to thank all the faculty, staff and students who lend their time and energy to the various admissions and outreach events. With their expertise, the admissions process is able to continually improve and further NUS Medicine's vision.



What it takes to mount the annual selection exercise for Medicine applicants.

University Scholars Leaders Symposium: Broadening Horizons and Empowering Future Health and Sustainability Champions

Held from 1 to 4 August 2023 at the United Nations Conference Centre in Bangkok, Thailand, 500 representatives from 46 nations came together at the 11th University Scholars Leaders Symposium (USLS) to learn from experts and each other, with the aim to spearhead sustainable initiatives for their communities.

In line with the School's aim to nurture empathetic medical professionals who are socially conscious, globally aware and committed to serve, the Office for Students (OfS) nominated and supported three medical students to represent Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) at the symposium. By offering our medical students with

learning opportunities that go beyond academics and the chance to be a part of a global community of compassionate changemakers, OfS hopes to spur our students into coming up with innovative solutions for the future of health.

NUS Medicine students Tammy Yim, Nathan Edward Lee and Sri Priyanka d/o Rajanala reflect on their experience.

Photo:
Participants at the 11th University Scholars Leaders Symposium.





NUS Medicine students Tammy Yim Si Yue, Nathan Edward Lee Jian Liang and Sri Priyanka d/o Rajanala at the Wat Arun Ratchawararam Ratchawaramahawihan temple in Bangkok city.



Many of the speeches were incredibly moving not just in their content, but also in the medium through which they were delivered. This made me realise how, often, the skills to pitch and share one's ideas are inextricable from the growth and success of any initiative. This important skill is not one to be overlooked, and I was privileged to have witnessed a range of great speakers exemplifying it throughout the symposium."

Tammy Yim Si Yue, Year 3 Medical student



This experience has ignited a fervent passion within me to continue serving my community in school and beyond. The symposium's focus on self-development and servant leadership resonated with me on a personal level. The enthusiasm I feel for working with the youth and my commitment to self-improvement have been further invigorated. I am determined to channel the inspiration I gained from the symposium into concrete actions that contribute to the betterment of society."

Nathan Edward Lee Jian Liang, Year 2 Medical student

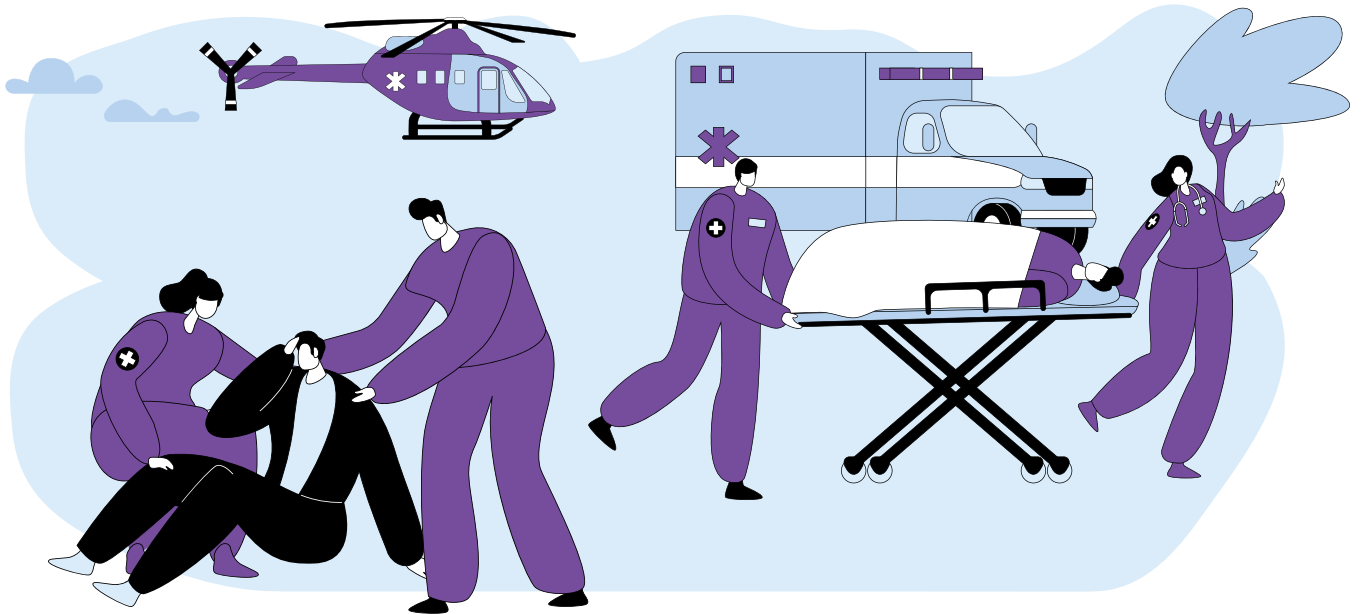


NUS Medicine student representatives with other delegates and speaker Ifrah Ahmed (Founder, Ifrah Foundation, Somalia).



I was inspired by the stories of humanitarian workers who had successfully integrated cultural sensitivity into their projects, resulting in more sustainable and impactful outcomes. This lesson reminded me that while technical skills are essential, cultural competence is equally crucial in the humanitarian field."

Sri Priyanka d/o Rajanala, Year 2 Medical student



Understanding Disaster Medicine

BY DR LENARD CHENG, ADJUNCT ASSISTANT PROFESSOR, DEPARTMENT OF SURGERY AT NUS YONG LOO LIN SCHOOL OF MEDICINE, AND CONSULTANT, EMERGENCY MEDICINE DEPARTMENT, NATIONAL UNIVERSITY HOSPITAL

NUS Medicine alumnus Dr Lenard Cheng shares about his fellowship year in Boston, US.

Our careers in Medicine often develop in stages. There's always some uncertainty moving from one stage to the next—the final year students will probably relate most with Postgraduate Year 1 (PGY1) looming behind the Bachelor of Medicine and Bachelor of Surgery (MBBS) exams. There are many stages after that, and I believe demystifying them will at least help build awareness and decrease anxiety. Previewing future

opportunities may even guide aspiration and strategy, so here's a peek into my own experience.

Just before I was appointed Consultant in Emergency Medicine, I spent a year on a fellowship in Disaster Medicine at Beth Israel Deaconess Medical Center, Boston, Massachusetts, US.

Disaster Medicine? What's that?

Depends. Who's asking?



The 2013 Boston Marathon Bombing. Boston is an affluent, metropolitan city that mostly enjoys peace—not unlike Singapore—until the 2013 bombing shook the community to its core. From the tragedy rose many initiatives to prepare for disasters. Image credit to "The Boston Globe".

Conceptually, Disaster Medicine is the provision and promotion of health in the context of disasters. We augment healthcare resources and capability, which we know will be exceeded during disasters. Disasters have always existed, some level of healthcare has always been provided, but resources have and will always be overwhelmed. Therefore, Disaster Medicine seeks to minimise need, maximise resources, and make up the shortfall.

Here's a contextualised example: Today, a bomb goes off nearby and 300 casualties flood into the hospital. What do medical students do? Probably not much. What can medical students do? Are they a potential resource to increase the hospital's disaster response capacity? How do we prepare them and alter the system to capitalise on that? This is one of many series of questions Disaster Medicine experts seek to (and have partially managed to) answer.

Organisationally, Disaster Medicine is, in most places, a subspecialty of Emergency Medicine. That's because many of the concepts, skills, and approaches are shared by the two disciplines. If you like acute care medicine, decision-making, system-tweaking, cross-discipline and cross-industry interactions, you might like Disaster Medicine.

What's the relevance for Singapore?

It's true and fortunate that our society has been spared from disasters. However, our flourishing petrochemical, aviation, port, and other industries, supported by critical



infrastructure that inevitably ages, are potential sites and origins of tragic stories.

Did you know, our Ministry of Home Affairs also considers terrorism threat to us to be high? Apart from conventional armed assaults, healthcare cyberattacks are an increasingly common and even more deadly threat.

What's a Fellowship?

A period of subspecialty training. While it is common for medical students to know about the specialty options post-medical school, subspecialties are usually esoteric and become relevant only after practising as a specialist.

You might choose to specialise in Emergency Medicine after graduating, rotating through the emergency department, and liking shift work, resuscitation, and short-contact-point practice. You'll look for a subspecialisation only after practising as an Emergency Physician and finding a niche beyond conventional Emergency Medicine.



Top:
Pre-deployment course: We set up camp in the mountains an hour away from the city, built fires, ate rations, simulated hostile scenarios, and practised some medicine.

Bottom:
Massachusetts state-wide full-scale exercise: More than 200 pre-hospital providers, including two helicopters, responded to a radiation dispersal device.

Does everyone go overseas for Fellowship?

Not necessarily. If the subspecialty you're choosing is based on locally rare presentations (toxicology) or situations (disasters), and it is still locally important, an overseas training ground becomes an important option.

What was your experience like? What cool things did you see over there?

Medicine in Boston has more similarities than differences from Singapore. There are even a good number of things we take for granted that they can learn from. That aside, the world's a big place, and my year was too short to exhaust all the eye-opening things that exist out there.

Several factors make Boston a mecca for Disaster Medicine. Its wealth provides resources, peace provides opportunity, and the scar of the 2013 Marathon bombing is impetus for authorities, healthcare providers, and the community to invest in disaster preparedness. For example, the 2023 Boston Marathon race organisers spared no effort to plan for the sporting event and mass gathering, and to prepare for disasters. We were invited to review and implement trauma stabilisation points that were worked into the plans of the hallowed Boston Marathon.

In a similar vein, public agencies like Fire, hazardous materials (HAZMAT), Police, and Emergency Medical Services of Central Massachusetts participated in a full-scale exercise of epic proportions that we planned. All 200 personnel, countless apparatus and equipment showed up to



respond to an explosion that the fellowship simulated with 100 live casualties. Behind the scenes were months of planning, scientific review, meetings, and storyboarding to ensure the drill was rigorous and realistic.

We weren't always in the driver's seat. We had our fair share of riding along on adventures. The Fellowship's flagship event is its pre-deployment course, three days of hands-on learning to operate in austere, and foreign environments. Humanitarian Medicine and missions span many levels, and one might be lulled by short, relatively peaceful, and comfortable trips to think that a willing heart is the only requirement. On the contrary, some humanitarian efforts can be the most gruelling and dangerous endeavours one must be properly trained for.

My deep-dive into Disaster Medicine opened a community of practice that collectively pushes boundaries. I was a beneficiary of this international Disaster Medicine community, having been invited to

participate in workshops and conferences, and to collaborate on research projects. In return, I had the opportunity to give back and strengthen the field by speaking at international conferences, developing think-tanks, and leading international teams in research and product development. Relevant to medical students, the World Association of Disaster and Emergency Medicine (WADEM) is one of the largest, if not the largest, societies of Disaster Medicine and has a Student and Young Professional Special Interest Group you can join!

I lived a whole life in parallel with my work, making new friends, exploring (many) new places, and experiencing the seasons. Who knew Emergency Physicians from various countries would tell different versions of the same emergency department horror stories! I would not hesitate to say that my year in Boston may be the best I have experienced. Special thanks to NUS Yong Loo Lin School of Medicine-NUHS-Harvard-BIDMC Programme for the joint sponsorship.

↑
Left: Counter Terrorism Preparedness Network high-level conference: International experts on counter terrorism gathered in Washington D.C. for this two-day conference.

Right: Graduating as Research Fellow of Harvard Medical School; some reverence is due given the prestige that the University built.

The Era of Extended Reality (XR) in Healthcare: Are Hospitals Prepared for the Future?

Photo:
HoloMedicine in the operating theatre.



THE BANYAN TREE

This column is dedicated to the pursuit of continuous learning and development and takes its name from the banyan tree. It has roots that grow deep, anchoring it firmly in the soil. The tree spreads its shade wide and far and provides space for reflection and discussion. We invite you to come and take a seat under its shade.

The Age of Extended Reality (XR) has dawned, and it is set to gain momentum in 2024. With improved XR devices such as Meta3, Vision Pro, and successors to the HoloLens, this technology is poised to make significant strides in healthcare. However, the critical question that arises is whether hospitals are adequately prepared for this technological transformation. From a global perspective, the answer appears to be a resounding "no." Fortunately, there are exceptions, and we'll explore them here.

How should a hospital prepare?

There remains a prevailing illusion that modern IT can be ensured in hospitals through on-premises solutions, i.e., local server installations. Recent cyberattacks on renowned hospitals in Germany have often been attributed to outdated infrastructures. Modern XR applications require stable cloud environments capable of automatic scalability. Here, keywords like Kubernetes, GPU, Defense-In-Depth, AI segmentations, generative AI, and Copilot come into play. A scalable cloud is the prerequisite. Secondly, hospitals need a private 5G network with low latency and speeds exceeding 700 megabits in operation rooms. While these may require significant investments, they are crucial for shaping the future of medicine and ensuring a hospital's



competitive advantage. 5G can secure a cloud, as every XR device, robot, or laptop is equipped with a 5G SIM card that protects against unauthorised access, providing precise access control.

Third, hospitals need medically certified applications, which the HoloMedicine® platform offers. It allows for the deployment of new upgrades and certification of new medical use cases every three months. Furthermore, it empowers hospitals to maintain independence, foster innovation, and integrate external suppliers like medical manufacturers into their architecture. Costs are kept fair and consumption-adjusted through cloud and SaaS solutions.

What are the use cases enabled by this triad?

Picture this scenario: Medical professionals no longer rely on laptops but wear lightweight XR glasses, enabling them to work hands-free. They can overlay patient information, surgical procedures, avatars, and more, streamlining their workflow. Assistant doctors have virtual senior doctors by their side, even when those seniors are at home. Doctors collaborate across distances like a virtual tumor board. Patients can virtually join their doctor at the hospital while remaining in the comfort of their homes. During surgery, the virtual CT scan is superimposed on the patient, enhancing precision and quality. Meanwhile, medical students utilise holograms to accelerate their learning. All these advancements enhance patient safety and quality of care.

A scalable cloud is the prerequisite. Secondly, hospitals need a private 5G network with low latency and speeds exceeding 700 megabits in operation rooms. While these may require significant investments, they are crucial for shaping the future of medicine and ensuring a hospital's competitive advantage.





Discussing a surgery procedure with a patient.

A programmatic approach to progress

Singapore is poised to be the hub of this future. Collaborations between apoQlar, Singtel, Microsoft, NUHS, and NUS have already introduced and implemented this technology. Over 150 user cases have been identified and are being gradually implemented, and other hospital chapters in Singapore are joining the movement. Hospitals from around the world visit Singapore to witness the solution in action. Importantly, policymakers are recognising the importance of this transformation. In the field of medicine, holograms will become more crucial than self-driving cars or any other innovations. It's no longer about hospital walls; it's about the IT infrastructure. The future is here, and those who lead it will shape the course of healthcare for years to come.

In conclusion, the advent of XR in healthcare is inevitable, and its impact promises to

In the field of medicine, holograms will become more crucial than self-driving cars or any other innovations. It's no longer about hospital walls; it's about the IT infrastructure. The future is here, and those who lead it will shape the course of healthcare for years to come.

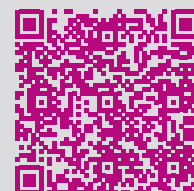
be transformative. Hospitals must prepare themselves by embracing scalable cloud environments, establishing private 5G networks, and adopting medically certified applications. These preparations will usher in an era where healthcare professionals work seamlessly with XR devices, ultimately improving patient safety and quality of care. Singapore serves as an example of what is possible when industry leaders and policymakers come together to drive innovation in healthcare. The future of medicine is now, and it's up to hospitals to lead the way.

To gain a deeper understanding of XR and Holomedicine and

explore the fascinating facets of digital health, join us in our two-day DTX HealthSG Leadership masterclass. Designed for visionary healthcare and business leaders, this immersive event is curated by NUS Medicine Continuing Education and Training. It offers a deep dive into sustainable growth strategies within Singapore's dynamic HealthTech realm.

Credit: VSI HoloMedicine®, apoQlar

Scan to register or for more details on the two-day masterclass



Take 5: Q&A with DTX HealthSG Leadership Masterclass 2024 Speakers



Mr Sirko Pelzl, CEO apoQlar and
Chairman HoloMedicine®

Q: What is the central theme of your presentation at the DTX HealthSG Leadership Masterclass 2024?

A: My topic revolves around the transformative potential of Extended Reality (XR) in healthcare. I will discuss how XR devices like Meta3, Vision Pro, and HoloLens successors and HoloMedicine® are revolutionising the industry, along with the necessary preparations hospitals should undertake. Additionally, I will highlight the real-world implementation of this technology in Singapore as a case study.

Q: What are the three main insights that attendees can anticipate gaining from your talk at DTX?

- A:**
- Insights into the pivotal role of XR technology in improving patient safety and quality of care.
 - Understanding the essential prerequisites for hospitals to harness the full potential

of XR, including cloud scalability, private 5G networks, and medically certified applications.

- Real-world examples of XR implementation in healthcare, with a focus on Singapore's success story and the involvement of various hospital chapters.

Q: How does your topic align with prevailing trends and challenges in healthcare, and why is it of importance to professionals and leaders?

A: XR technology is at the forefront of healthcare innovation, aligning with the global trend of leveraging cutting-edge technology to enhance patient care. Professionals and leaders must be knowledgeable about XR's potential to stay competitive

and provide top-tier healthcare services. As healthcare becomes increasingly digital and remote, XR offers an unparalleled opportunity to bridge gaps in patient-doctor interactions and medical education.

Q: Share an interesting fact related to your presentation topic.

A: Did you know that XR technology has the potential to reduce the need for physical presence in medical training and surgeries, making it possible for medical students to learn from the best practitioners globally and for doctors to collaborate seamlessly across vast distances? This fact underscores the revolutionary impact XR is poised to have on the healthcare landscape.





Professor Lim Chwee Teck, NUS
Professor and Director of the Institute
for Health Innovation and Technology,
National University of Singapore

Q: What is the central theme of your presentation at the DTX HealthSG Leadership Masterclass 2024?

A: Advancing Healthcare through Technological Innovation.

Technological advancements have been pivotal in advancing the field of health and healthcare. Without such innovations, we will not have our modern-day hospitals and healthcare facilities. Beyond just facilitating improved diagnosis and treatment, health technologies have also contributed to prolonging lifespan and enhancing overall health. Here, I will showcase how some of the emerging health and medical technologies are going to transform and impact the way patients are going to be diagnosed, treated and monitored. As we enter into the era of personalised medicine, these technologies will ensure that the future of healthcare will not only be about timely diagnosis and precise treatment, but also prevention.

Q: What are the three main insights that attendees can anticipate gaining from your talk at DTX?

A:

- How technological innovations are the backbone of modern

healthcare, going beyond diagnosis and treatment to extend lifespan and enhance overall health.

- Emerging health technologies are set to transform healthcare, by shifting its focus from hospital to home and focusing on personalised and preventive medicine.
- This dynamic evolution in healthcare underscores the profound impact of technology on patient well-being and quality of life.

Q: How does your topic align with prevailing trends and challenges in healthcare, and why is it of importance to professionals and leaders?

A: Understanding emerging health technologies is vital in healthcare due to their impact on patient care, personalised medicine, preventive healthcare, and system efficiency. Healthcare professionals and leaders must grasp these innovations to deliver precise treatments, promote patient-

centric care, manage costs effectively, and ensure equitable healthcare distribution. Staying informed about these technological shifts is crucial for delivering high-quality, adaptive healthcare in a constantly evolving landscape.

Q: Share an interesting fact related to your presentation topic.

A: Health metaverse that harnesses virtual reality (VR), augmented reality (AR) and artificial intelligence (AI) are increasingly being explored for applications in healthcare. For example, such an approach has great potential for use in medical training, rehabilitation and even psychotherapy. The use of these immersive technologies for healthcare is not only innovative and transformative, but also showcases how such futuristic tech can lead to better healthcare delivery, accessibility and personalisation, thus making it more efficient, cost-effective and sustainable.

Mark your calendars for 9 – 10 May 2024, and prepare to embark on a two-day journey delving into the theme of SG Health Transformation and the future of digital health. We're bringing together leading experts to share their groundbreaking insights with you. Simply scan the QR code to register and seize your opportunity to enjoy special discounts!



MSc / Executive / Short Courses Certificates

CHARTING A PATH TO SUCCESS IN HEALTHCARE INNOVATION



**Register
for Our
2024 Intake
Now!**

Available Courses

MAY 24 INTAKE

- ▶ Driving Innovation in Healthcare

AUG 24 INTAKE

- ▶ Executive Certificate in Healthcare Improvement via Informatics
- ▶ Master of Science in Biomedical Informatics (MSc in BMI)

About Us

At NUS Medicine Continuing Education and Training, we offer training programmes to professionals and organisations to acquire existing and emerging skills and expertise to meet the needs of the healthcare sector of tomorrow.

For enquiries on courses, please contact:

- General Course Enquiries:
nusmedcet@nus.edu.sg
- MSc in BMI Course Enquiries:
nusdbmi@nus.edu.sg



Yong Loo Lin
School of Medicine

**Inspiring
Health For All**

**NUS Yong Loo Lin
School of Medicine**
1E Kent Ridge Road
NUHS Tower Block, Level 11
Singapore 119228

Email medcomms@nus.edu.sg
Web medicine.nus.edu.sg

Follow us on



[@NUSMedicine](#)



[@NUS Medicine](#)



NUS Yong Loo Lin
School of Medicine