02 ISSUE | JULY 2015

Dean's Message

In my first official week as Dean, I appreciate this opportunity to share my thoughts about Duke-NUS, where we have been and where we are going.

In the relatively short span of ten years, Duke-NUS has accomplished great things and has built a solid foundation for future achievement.

During this time, we have graduated five classes of MD students, and our first MD/PhD and PhD students finished up their studies this May.

These graduates are the product of the innovative programmes of our Education team. Our pioneering TeamLEAD learning model, anchored on self-directed learning, continues to impress and inspire educators and institutions here and abroad. More expansive learning and teaching innovations are on the way. A number of these innovations are featured in this issue.

On the research side, our faculty has also been innovative and productive – over 2,000 papers have been published in international peer-reviewed journals; over 40 national research awards* have been garnered, and collectively, over S$290 million research funding have been raised locally and overseas.

Recently, two breakthrough studies on dengue were published in the prestigious journal Science. This work by Duke-NUS investigators is very likely to enhance the clinical treatment and prevention of dengue and accordingly, was well-covered by the media. As such, this research reflects our school's strong commitment to finding better treatments for diseases of concern to Singapore and our region.

I am very excited about assuming the role of Dean at Duke-NUS. This presents a rare opportunity to work with an outstanding group of individuals. From our students who continue to impress with their scholarship and academic achievements as well as heartfelt, dedicated efforts in community service, to our faculty and staff with their terrific 'will do and can do' spirit.

It will also be a privilege to work with our partners at SingHealth as we continue to develop the SingHealth Duke-NUS Academic Medical Centre. The AMC provides a requisite vehicle for our education and translational research programmes, allowing full expression of our efforts to positively impact patient care here in Singapore.

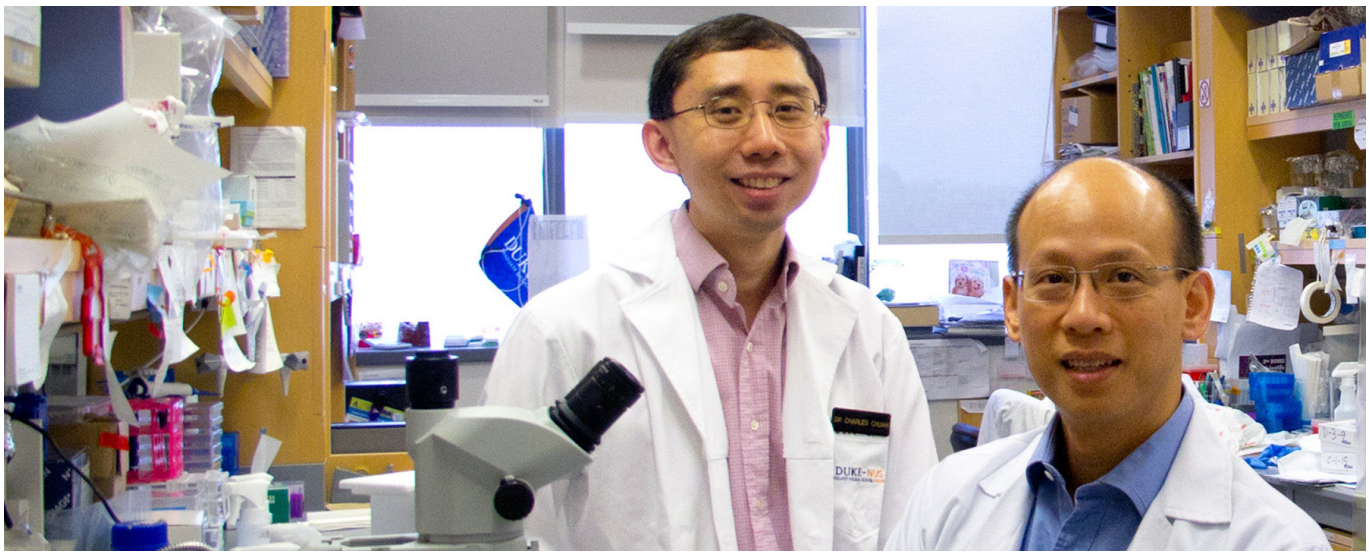
I also look forward to working with our dedicated Governing Board, consisting of stakeholders and prominent individuals from our community, who donate their talents and valuable time to help us achieve our objectives of transforming medicine and improving patients' lives.

Finally, I want to acknowledge and thank Professor Ranga Krishnan, who has provided superb leadership as Dean of our school over the past seven years. The myriad achievements of Duke-NUS during this time are a testimony to his creative thinking and exceptional abilities as a leader. I also want to personally thank Ranga for his generosity and wise mentoring during my transition into this job. I will certainly do my best to build on his impressive legacy.

With best wishes,

Thomas Coffman, MD
Dean

**MOH NMRC research awards: Singapore Translational Research (STaR) Investigator Awards, Clinician Scientist Awards and Transition Awards*



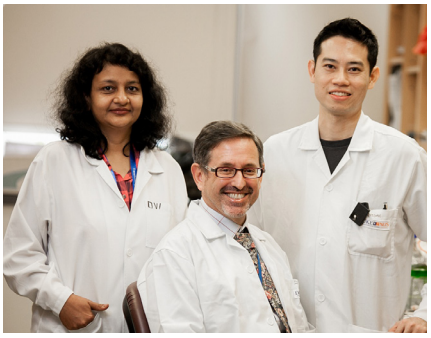
Asst. Prof. Charles Chuah (left) and Assoc. Prof. Ong Sin Tiong

COLLABORATIONS FOR PRECISION

One size does not fit all – least of all in medicine where body chemistry, genetics and disease variants affect the effectiveness and outcome of treatments. At Duke-NUS, collaborations made under its Academic Medicine umbrella have accelerated results and more efficient outcomes.

Precision is the new watchword in medicine. After all, conventional one-size-fits-all therapeutic strategies are not equally effective in all patients and may even cause undesirable side-effects. Cancer provides clear examples of why precision is important. Research shows that cancers that look the same may be genetically very different, so the same treatment may not work for everybody. A more targeted approach not only avoids ineffective treatments, unnecessary ill-effects, and poor use of resources, but also translates to better outcomes and quality of life for patients.

Dr. Cheong Jit Kong, like many of his colleagues in the Duke-NUS Cancer and Stem Cell Biology (CSCB) Programme, has leveraged the Academic Medicine approach within the school as well as with other institutions, such as SingHealth and A*STAR, to further the pursuit of more personalised medicine. This approach, he observed, unifies the spectrum of medicine, from clinical care to scientific research and knowledge sharing. "The union of these aspects of academic medicine has allowed physicians and physician-scientists to identify key clinical problems, resolve them via rigorous scientific investigation and translate these solutions to improve treatment outcomes," he said.



Researchers from the Virshup lab (from left): Asst. Prof. Babita Madan, Prof. David Virshup (seated) and Dr. Cheong Jit Kong

Overcoming Resistance, Improving Targets

Take certain cancers such as non-small cell lung cancer and chronic myelogenous leukemia (CML) for instance. A CSCB research team has found that a specific gene mutation in these cancers lead to drug resistance. Dr. Ong Sin Tiong, Associate Professor, CSCB explained, "We have found that some cancers occurring in patients who have inherited an East Asian-specific variant in the 'BIM' gene are less likely to respond to standard therapy. We are studying to see if we can add additional drugs to the standard treatment so we can overcome the resistance conferred by the gene variant."

One of the potential drugs that CSCB and SingHealth researchers are testing in the treatment of CML is pyrvinium, an FDA-approved drug with a known safety record in human patients. This drug is able to specifically kill cancer cells without harming normal cells. It can also – when combined with another drug – be used to block cancer promoting-pathways. This work was made possible through the close collaboration with Professor David Virshup, Programme Director of CSCB as well as with Dr. Charles Chuah, Assistant Professor, CSCB and Director, Department of Clinical Research, Singapore General Hospital. "It is every clinician-scientist's aim to translate findings from the bench to the clinics for the improvement of patient care," shared Dr. Chuah.

The Academic Medicine partnership between Duke-NUS and SingHealth, has provided the ideal environment and tools to make this possible. It integrates three functions of medicine - clinical care, education and the development of new knowledge - to close the gaps between research

and academic discovery, and deliver solutions to patients.

The CSCB team has leveraged Dr. Chuah's established platforms to evaluate cancer stem cell activities, while his lab enables access to a large repository of patient samples. Researchers at CSCB, such as Dr.Cheong, provide the expertise to identify the anti-cancer drug targets. Together, they are able to find alternative treatment strategies at an unprecedented speed.

Different Pathways to Treat Known Cancers

In a similar quest to better target cancer, Prof. Virshup's lab has exploited unique genetic weak spots in some pancreatic and colon cancers, thanks to effective collaborations. The Virshup lab has had a multi-year collaboration with A*STAR's Experimental Therapeutics Centre and D3 (Drug Discovery & Development), both headed by Professor Alex Matter.

Preclinical animal studies have found that inhibiting an enzyme known as 'porcupine' or PORCN prevents growth of certain cancers. "PORCN plays an essential role in a signalling pathway called Wnt that is responsible for cell to cell communication and growth control," Prof. Virshup said. "All human Wnts require PORCN for their activity, suggesting that inhibition of PORCN could be an effective treatment for cancers dependent on excess Wnt activity."

Academic Medicine Spurs Results

These are but a sample of outcomes from the CSCB programme – but each underscores the importance of collaboration in the search for targeted treatments. By working in parallel and with the benefit of tapping the expertise of peers in both research and clinical environments, discoveries can be made with greater speed, precision and efficacy. Dr. Ong added, "Modern medical research is a team sport; to do it effectively you need collaboration from patients, clinician-scientists and clinicians."

DUKE-NUS: TEN YEARS ON, REDEFINING MEDICAL EDUCATION

"To improve the way education is delivered, we are committed to continuous improvement to ensure that our systems are flexible, responsive and relevant."
- Assoc. Prof. Sandy Cook

The Continual Revolution

Developing a truly innovative medical education model is a constant process of reflection, improvement and responsiveness. New educational innovations at Duke-NUS will enhance medical training to nurture more well-rounded doctors.

The idea of transformation and improvement is not just reflected in Duke-NUS' mission statement, but in the continued efforts to improve the way education is delivered. In a medical landscape marked by constant and rapid change, it is imperative to do so, observed Associate Professor Sandy Cook, Senior Associate Dean, Education. "Our goal coming in is to be a catalyst for change," she said, "To do this we are committed to continuous improvement to ensure that our systems are flexible, responsive and relevant." This is important in light of changing patient profiles and healthcare delivery models. For instance, moves are in place to evolve TeamLEAD – Duke-NUS' signature approach adapted from team-based learning – to not just getting students to prepare before class, but to proactively address their knowledge weaknesses using technology before the start of classes. Pilot schemes, said Professor Robert Kamei, Vice Dean, Education, are underway to look into personalising education more so that students are able to progress at a pace appropriate to their specific skills, abilities and learning progression. This approach aids educators in identifying the concepts or topics that a student is weak in, and provides inputs to help him/her address those gaps.

Connecting Clinical Practice to People

Going forward, moves are in place to build an even more robust programme, with a particular focus on improving the more clinical parts of the education and becoming more patient-centric. "We want to develop the whole person: a caring physician who has the clinical skills but one who also can connect with patients as people," Dr. Kamei said. "By developing a programme that is holistic, we develop people-centred medical professionals who will be able to align with the patient-centred healthcare model that is becoming increasingly important."

For instance, a typical clinical rotation – a system that has remained unchanged for generations – has medical students spending months on a different specialty in the hospital wards. "While this model has not changed, medicine, the type of illnesses and disease management has changed," Dr. Kamei said, pointing out, "More and more, patients are managed

Leading the way to redefine Duke-NUS education (from left): Assoc. Prof. Sandy Cook, Assoc. Prof. Scott Compton, Assoc. Prof. Silke Vogel, Prof. Robert Kamei and Assoc. Prof. Ong Sin Tiong

outside of inpatient wards, especially for those with chronic illness who may require different levels of care." The conventional rotation means many medical students only see patients in the acute stage, which reflects only a small aspect of their overall illness, and miss out on the continuity of care, he elaborated. Addressing this is a new pilot Longitudinal Integrated Clerkship (LIC), aimed at exposing students to patients over a more sustained period so they have a better understanding of the 'person behind the patient' and the 'story' beyond the disease. This, Dr. Kamei explained, imparts not just a more comprehensive practical clinical knowledge, but also maintains empathy and a patient-centric ethos.

Complementing the LIC is the LIFT grant, a technology and education grant given by NUS that will enable Duke-NUS to create technologies that will help students connect with people and their lives in their community. Like the LIC, it helps give medical students a more comprehensive idea of the people they treat.

"It is important for medical students to understand the greater context: that patients are people first," Dr. Kamei emphasised. One of the biggest missing links in medicine is that while patients within a hospital or clinic setting get the right diagnosis and medicine, they may not always be able to comply with treatment. There may be a multitude of reasons why patients may not take the prescribed medication, not because they refuse to but rather the lack of clear instructions and in some cases those who are unable to afford the medication. Doctors need to look at the bigger picture, Dr. Kamei pointed out, and appreciate that each patient's background, families, cultures, social-economic, circumstances, language proficiency and community all matter. "These have a huge impact on how that person manifests a disease, the way they manage their illness and comply with treatment," he said. "This understanding, this connection with people and not just disease, helps our students be better, more empathetic doctors. It also helps them remember the reasons they enter medicine in the first place. Education has to start connecting medical students with people so that healthcare delivery is not purely transactional but holistic."

"By developing a programme that is holistic, we develop people-centred medical professionals who will be able to align with the patient-centred healthcare model that is becoming increasingly important."
- Prof. Robert Kamei

Balancing Skills

Sustaining the passion for medicine despite its challenges – the long hours, high-pressure situations, life-and-death scenarios and more – underscores the importance of nurturing a better doctor with not only the right education, but the right life skills. "We also want to equip our students with the resilience to avoid burn out and lack of empathy, so that they can be happier, healthier and as a result, better doctors," Dr. Kamei explained, "As a school we have some responsibility to give students the skills to cope with the ups and downs that are inevitable in the medical profession." Jennifer Davis, Director, Student Wellness, and Assistant Professor Mara McAdams, Assistant Dean for Student Affairs are developing programmes to equip students with the skills needed to cope with stress in a healthy and positive way, to become more empowered as individuals and as doctors.

Connections that Matter

To make a difference not just as a school and internally, but to drive sustained and holistic impact, it is also essential to integrate Duke-NUS' educational ethos with the wider health and education system. This is where the Academic Medicine Education Institute (AM•EI) comes in, Dr. Cook said, an institution designed to support innovative

pedagogical approaches and nurture a culture of teaching and learning that is open to curiosity and asking questions. Doctors have always been expected to impart their medical knowledge, but they may not necessarily have been taught how to be a good teacher. The AM•EI is a way of advancing medical education by giving doctors the skills and knowledge to be better educators and mentors. Dr. Kamei said, "As a community the AM•EI is one where teachers can come together, support each other and share solutions. This means not just working harder and faster, but more importantly, more effectively as teachers."

Ultimately, these moves as a whole are aimed at transcending the traditional approach of education going beyond merely conveying of skills and knowledge, but nurturing an environment where students and practicing clinicians receive and transmit medical knowledge as well as develop a holistic approach towards medical education.

For more information on education at Duke-NUS, please visit: www. duke-nus.edu.sg/education

A CONTINUED VISION OF IMPROVING EDUCATION

Ten years on, education at Duke-NUS is at an exciting crossroad. Two of Duke-NUS Heads of Education share their thoughts on the milestones and future plans for the various programmes at Duke-NUS.

"Today, education is no longer a one-size-fits-all train barrelling down the tracks, oblivious to students who lag or race ahead. We are at the dawn of a new age in education; learning how to harness technology to help us provide adaptive educational strategies to promote and individualise learning. Technology has enabled us to track students' learning and use that information to provide the right content at the right level and at the right time to each and every student. It's truly exciting to see some of this work developing. As for the TeamLEAD teaching programme, I hope to not only continue to drive its efficiency as a tool for teaching medicine, but also use it to generate impactful educational research that improves our understanding of how people learn. My goal is to grow our research portfolio by promoting a supportive academic environment that inspires our faculty to conduct educational research."

- Associate Professor Scott Compton, Associate Dean, Medical Education, Research and Evaluation

"This year's graduation marks a special event – we are not only celebrating ten years of Duke-NUS but also, a special milestone for the IBM (Integrated Biology and Medicine) PhD programme as our first PhD students graduate. In 2010, they started in a newly-minted programme. I believe they have discovered that biomedical research really is 'rocket science' because the road is long, winding and at times littered with rocks. But by being deeply engaged they have overcome obstacles, pushed boundaries and found new discoveries. It has been an incredible journey for all of them. Over the past five years, the PhD programme has matured, with dedicated research faculty mentoring our students and students excelling at their projects. Looking forward, we aim to provide more avenues for students to stay up-to-date with new research approaches and technologies as well as explore professional and career opportunities under the new Career Development Programme."

- Associate Professor Silke Vogel, Associate Dean, Graduate Studies

MARCHING TO THE BEAT OF A DIFFERENT DRUM

The ability to seamlessly traverse the interconnected worlds of medicine and science, and make discoveries that can 'transform medicine and improve lives', requires a unique skillset found among individuals who march to a different beat. These individuals are doctors with training in the disciplines of both medicine and scientific research – MD/PhDs who can function as the nexuses between clinical medicine and bench-based research.

Duke-NUS' MD/PhD course is designed to train just this sort of doctor on the quest to be a medical 'transformer', providing a four to five year PhD component within their medical training. This prolonged and intensive research experience develops and equips students for a career in translational research, according to Associate Professor Ong Sin Tiong, Director of the Duke-NUS MD/PhD Programme Office

"The MD/PhD programme imparts a very potent and specialised combination of skills. Our students are trained to not only be clinicians but also professional researchers," Dr. Ong explained. "Trained right, our MD/PhDs will be well-placed to identify the gaps in healthcare, pose important clinical questions, as well as formulate research strategies to address these gaps. This is particularly true for practice-changing, high-impact discoveries, since this level of work usually requires the collaboration of multi-disciplinary teams of clinicians, health services and outcomes researchers, and laboratory-based scientists. Through instilling our MD/PhDs with an intimate understanding of clinical issues and equipping them with laboratory and analytical skills, we hope to enable them to be effective leaders of such teams, and realise our mission of transforming medicine and improving lives," he added.

"Through instilling our MD/PhDs with an intimate understanding of clinical issues and equipping them with laboratory and analytical skills, we hope to enable them to be effective leaders of such teams, and realise our mission of transforming medicine and improving lives."
- Assoc. Prof. Ong Sin Tiong

However, only a minority of doctors choose the MD/PhD route, since the training is long, arduous, and the results of their day-to-day experiments are often unpredictable. Those who are most suited, said Dr. Ong are those who 'delight in the process of discovery'. "They should have a deep desire to improve patients' lives, and possess an insatiable curiosity to understand how things work," he said, elaborating, "For these individuals, the long hours will fly by, and like the proverbial child on a long car journey, the question will shift from 'Are we there yet?' to 'Is it always this fun?'"

The MD/PhD Programme Office helps trainees on this journey by establishing and maintaining a vibrant and nurturing environment within the school, providing career advice and connections to the residency programmes and clinical departments, and matching students to world-class role models within the local environment. As for when success can be ascertained, Dr. Ong said, smiling, "Well, given the dedication and quality of our current MD/PhD students, it will only be a matter of time before they begin to transform the practice of medicine in our Academic Medical Centres. Perhaps then, others will also begin to 'catch the beat' and join us on this exciting journey!"

A Clinician-Scientist

Dr. Ong Sin Tiong is a haematologist and medical oncologist by training. He graduated with a medical degree from Cambridge University, and completed his clinical and subspecialty training at Cambridge University, the National University Hospital Singapore, and the University of Chicago. Prior to returning to Singapore to join Duke-NUS, he was on the faculty at the University of California at Irvine, where his work focused on understanding drug-resistance in haematologic malignancies. His laboratory work has received past and current funding from the National Institutes of Health, and the Lymphoma and Leukemia Society. Dr. Ong continues to see patients, and seeks to improve their care through the ongoing work in his laboratory.

Dr. Ong is also a member of the American Society of Hematology and American Society for Clinical Investigation, an honour society of physician-scientists. He has received several clinician-scientist awards, including from the American Society of Clinical Oncology, the University of California, and the Singapore National Medical Research Council, Singapore Ministry of Health.

MD/PhD graduate, Dr. Nicodemus Oey (left) with his mentor, Assoc. Prof. Antonius Van Dongen

Interesting Facts about the Duke-NUS MD/PhD programme:

- MD/PhD graduates are awarded two degrees: a Doctor of Medicine (MD) degree and a PhD degree in Integrated Biology and Medicine
- 19 students are currently enrolled in the Duke-NUS MD/PhD track (as at 1 June 2015)
- Dr. Nicodemus Oey is the first student to graduate from the Duke-NUS MD/PhD programme

"CARE will provide methodological training on how to generate useful data to enhance our knowledge of ageing."
- Assoc. Prof. Angelique Chan

CARE-ING FOR HOLISTIC AGEING

A new centre at Duke-NUS will strengthen Singapore's ability to better understand ageing issues, paving the way for impactful policies, solutions and care.

With ageing issues taking on greater prominence across the world and in Singapore, it is imperative to develop systems and institutions to tackle them holistically. According to Dr. Angelique Chan, a sociologist and an Associate Professor in the Signature Research Programme in Health Services and Systems Research (HSSR) at Duke-NUS, the key concept is to focus on ageing holistically, from a social and clinical perspective.

To this end, she has spearheaded the Centre for Ageing Research and Education (CARE), a new academic research centre that will conduct multi-disciplinary research on the social and medical aspects of ageing. CARE was announced at the 27th REVES Scientific Meeting which was graced by Senior Minister for Health and Manpower, Dr. Amy Khor. Dr. Chan pointed out, "A lot of focus tends to be around the clinical problems associated with ageing. However, the social – including social integration, productivity, lifelong learning, caregiving and environmental facets of ageing – are equally important in defining successful ageing."

The research at CARE will address eight different themes: healthy ageing; mental well-being; visual impairment in ageing; neurocognitive disorders in ageing; retirement; transition and health well-being; long-term care; caregiving; integrating health and community-based care. "It is an

Senior Minister of State for Health and Manpower, Dr. Amy Khor (centre, in black) was the Guest-of-Honour at the 27th REVES Scientific Meeting

opportunity to combine social and medical expertise in Singapore to provide high quality research evidence for policy makers," she added. "The centre will also provide methodological training on how to generate useful data to enhance our knowledge of ageing."

Projects in the Works

Already, researchers from HSSR and CARE are evaluating an intervention study called Ageing-in-Place (AIP) to address the resource-intensive needs of patients with chronic illness. The AIP scheme involves a network of community health nurses who help assess, monitor chronic conditions, and assess the social, medical, and rehabilitation needs of these patients. They also offer caregivers support in the home.

CARE is also conducting data collection for the third wave of a Panel on Health and Ageing of Singaporean Elderly (PHASE). This longitudinal study aims to develop a profile of the changes in physical, social and mental health of Singaporeans aged 60 and above.

Two new sequential cohort studies are in the pipeline. Together they will cover approximately 7,000 adults aged 50 and above. The enrolled study participants will be followed every two years and data will be collected on their social and physical well-being, which includes attitudes towards work and retirement, volunteerism and lifelong learning.

To date, CARE has completed three other studies. One was a survey on informal caregiving; the second was a study of factors that influence the use of long-term care services; and the third was an intervention study to determine if self-care education would be effective for older persons. The data from these and future studies provide a rich source of information and valuable insight into Singapore's ageing population to form the basis for more comprehensive and relevant policies, infrastructure and support systems.

For more information on the Centre for Ageing Research and Education (CARE) please visit www.duke-nus.edu.sg/care

REVES Scientific Meeting in Singapore and the Concept of Health Expectancy

The 27th REVES (Réseau Espérance de Vie en Santé) Scientific Meeting, held from June 2 to 4, 2015, brought together top international researchers to address the issue of 'health expectancy'. Unlike life expectancy, which is the measure of the length of life, health expectancy measures the quality of life and combines issues of mortality, morbidity, function and disability. It is an important shift in the development of holistic ageing-related policies and embraces the idea of not just adding more years to life, but adding healthy life years. Already this concept is part of age-related policies in the United States, the European Union and Japan. The 27th REVES Scientific Meeting was an opportunity to promote the concept in Singapore as well as the region. Speaking on issues of health expectancy were a wide range of ageing and disability experts such as University of Montpellier's Professor Jean-Marie Robine, who is also Research Director at the French National Institute of Health and Professor Saito Yasuhiko, Nihon University.

GRADUATION 2015: THE PURSUIT OF A CALLING

For the 49 Duke-NUS medical students who graduated in June 2015 – the fifth batch to do so since the school started in 2005 – the occasion was one marked by profound joy and a sense of accomplishment. The graduation ceremony also included the school's first batch of eight PhD graduates from the Integrated Biology and Medicine programme.

From top: MD/PhD graduate Nicodemus Oey in his commencement speech
MD graduates, Glenn Goh (left) and Olivia (centre) with their fellow classmates
MD graduate, Shayna Siew (right) receiving her MD degree from Guest-of-Honour Deputy Prime Minister, Mr Teo Chee Hean

Nicodemus Oey, the first to graduate from the MD/PhD programme at Duke-NUS, reflected that the seven years going 'off the beaten path' was well worth it. "Igniting the pioneering spirit is not an easy task and once ignited, keeping the flame burning takes a massive toll on one's psyche. Now that I have completed some of my formative training, it is my opportunity to show the world what I have learned as the first MD/PhD graduate in my efforts to improve medicine and transform lives," he said.

"Duke-NUS programmes' focus on translational science, recognise that advancements of medicine cannot exist without biology. Our faculty and students have strived to bring what we learn from basic science at the bench to clinical practice at the bedside."

- MD/PhD graduate, Nicodemus Oey

For Olivia Tan, who switched from a stable and comfortable career in finance, her graduation vindicated her decision to make such a major change. "Although there were times when I questioned the decision, and the transition was more difficult than I had foreseen, I believe I made the right choice. I came into medicine for the opportunity to help people and the promise of life-long learning. Medicine has definitely not disappointed in both these respects."

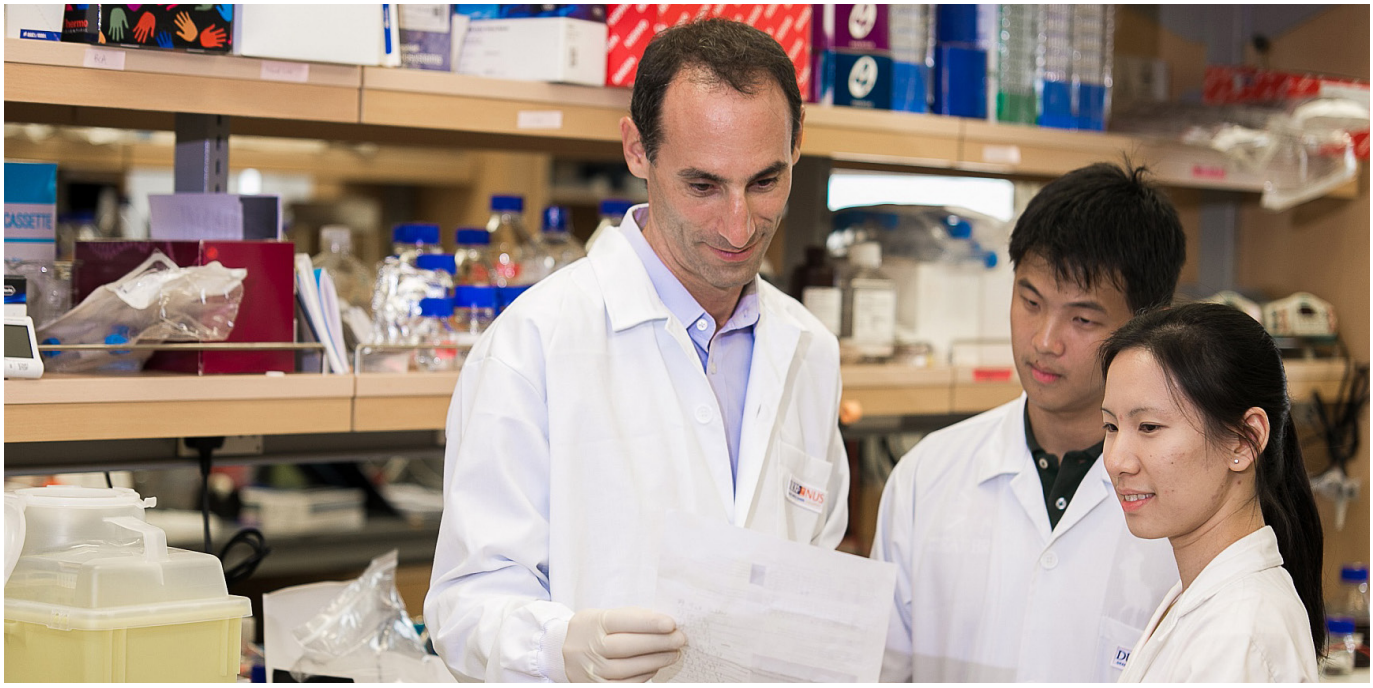
Shayna Siew, who likewise took a slight detour (she earned a degree in pharmacology before going to medical school), looks back on her decision with satisfaction. She will be going on to pursue a two month stint as a Global Health Fellow at Duke University Sanford School of Public Policy's Geneva Program on Global Policy and Governance before starting work as a house officer. She said, "Medicine has given me a front row seat in the lives of my patients. Although Singapore is known to be an affluent nation, there are many for whom medical care is still unaffordable or inaccessible, especially for the elderly, women and low skilled migrant workers. Medicine has not only brought new perspectives to my life, it has also taught me many life skills."

Her classmate, Glenn Goh, added that his medical school years cemented the reasons he pursued the calling in the first place. For one, his work with Dr. Tan Ngiap Chuan on a study to test the usage and uptake of the caloric-monitoring mobile health app iDAT (or Interactive Diet and Activity Tracker) helped him see how he could impact the lives of patients by understanding them. "We ask ourselves why we pursue medicine as freshmen and now at the end of my medical school journey before we start work as doctors, I revisit this question with more perspective," he said, "Fundamentally, we just want to help people. So for me, medicine not only equips me with the knowledge and skills to help people, but there's also an unspoken trust given by them to allow me to provide the help they need."

Our Cohorts in Numbers

Medical education at Duke-NUS – already unique in approach and design – is also distinct for other reasons. Here are some interesting facts about Duke-NUS MD and MD/PhD cohorts over the last eight years:

- Duke-NUS students hail from 24 different countries, bringing a diversity of skills, backgrounds and cultures to the community
- 43% of MD tudents were working before they started medical training at Duke-NUS
- 24% of MD students entered with non-science first degrees (pharmacy and nursing are classified under science degrees)
- 17% of the students have engineering degrees



MD/PhD student Vera (right) with her mentor, Assoc. Prof. David Silver (left) analysing her research findings.

TWIN PASSIONS: IN PURSUIT OF PATIENT-CENTRED IMPACT THROUGH NEW DISCOVERIES

The desire to do science and treat patients led Vera Goh to the Duke-NUS MD/PhD programme.

Vera Goh has always been torn between choosing medicine or science as a career. "As a doctor, you strive to improve one person's life at a time. In science, you hope to make discoveries that will contribute to the existing foundation of knowledge that future generations may benefit from," she reflected. This yearning to do both led her to pursue the MD/PhD route at Duke-NUS. "Both careers are equally meaningful and fulfilling, and it is my privilege to be given the opportunity to pursue both," she said.

The Best of Both Worlds

Her pursuit of both scientific enquiry and medical studies has taken her on a different path from most scientists and doctors. A typical MD/PhD programme takes an average of about seven to eight years. While a PhD student may enrol in a PhD programme directly after an undergraduate degree and complete the degree in approximately five years, Vera has dedicated her first two years at Duke-NUS studying medicine and is currently completing the PhD component. "I will then continue with my medical training and at a suitable time in the future, I will return to the laboratory to continue my scientific pursuits," she explained.

Being exposed to clinical work during the first two years in the programme is an important feature and has guided her towards her research interests. "The dual training as doctor and

scientist will hopefully enable us to identify important clinical problems that we can take back to the laboratory for further study," she said. The long MD/PhD journey is fraught with challenges, she acknowledged, but the series of discoveries along the way influences and propels her towards the next milestone. "I am continuously learning something new from my experiments that will eventually lead me towards certain scientific truths, big or small. For me, research is so interesting because it allows me to pursue a deeper understanding of the biological systems that make up living things."

Exciting Discoveries

Working with Associate Professor David L. Silver in the Cardiovascular and Metabolic Diseases Programme at Duke-NUS, she has had the opportunity to help him continue to uncover the functions of the Fat-storage Inducing Transmembrane protein 2 (FITM2) gene, a mutation Dr. Silver discovered in 2008.

"I was thrilled by the potential clinical impact I could make on the family harbouring this mutation. This inspired me to focus on my current area of research. Clinical relevance aside, it is simply exciting to work on a newly discovered gene/protein, and be the first person to uncover what it does at both the cellular and physiological level," she recalled. Significantly, she

"As a doctor, you strive to improve one person's life at a time. In science, you hope to make discoveries that will contribute to the existing foundation of knowledge that future generations may benefit from."
- Vera Goh

aims to better understand how a new clinical syndrome caused by the FITM2 null mutation, influences physiological changes. "By finding out what FITM2 is doing within a cell and at the organism level using both in vitro assays and mouse models, we can potentially come up with a treatment to improve this condition."

Wrong Turns to Find the Right Mark

Looking back at her years of work, countless false hypotheses, road blocks, unsuccessful leads and new clues, Vera feels a sense of accomplishment. She has come away with a strong belief in the scientific process. "We may have gone through countless hypotheses that turned out to be false, but these were still important to disprove," she said. "Eliminating these false leads also led to new clues that eventually pointed us in the right direction. We reached a turning point when all of a sudden things started to work because the hypothesis was the right one. It was not by luck or chance but by perseverance and keeping a level head that led us towards the right hypothesis."

Her advice to potential MD/PhD students? "Duke-NUS is a great place for aspiring clinician-scientists as students are exposed to ward rounds and medical conditions very early on in their training, before they join a research lab to pursue their scientific interests. I am glad to have chosen Duke-NUS as a platform for my future career, and would encourage students with a strong interest in clinical and scientific research to join our growing community."

Vera Goh entered Duke-NUS in 2009. She will be completing the PhD component of her MD/PhD programme this year. She will then continue with her remaining MD modules before applying to a medical residency of her choice.

Vera receiving the Young Scientist award from Prof. Ivy Ng (right), SingHealth Group CEO, during the 2014 SingHealth Duke-NUS Scientific Congress

Photo: SingHealth

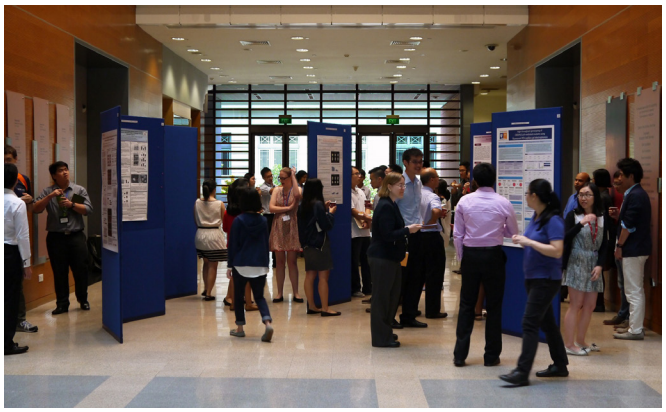
A DAY OF EXCITING RESEARCH: STUDENT RESEARCH SYMPOSIUM 2015

By Associate Professor Silke Vogel

On May 4, the Integrated Biology and Medicine (IBM) PhD programme hosted its second annual Student Research Symposium. It turned out to be a fantastic day where all our students showcased their impressive research projects, and engaged in lively discussions with faculty and research fellows. In addition, we were fortunate to host two world-renowned keynote speakers: Professor Andreas Strasser, Division Chief at the Walter and Eliza Hall Institute of Medical Research in Melbourne; and Associate Professor Chris Kontos, from the Department of Pharmacology and Cancer Biology at Duke University.

Dr. Strasser inspired the students with a brilliant presentation on his research and provided insights into programmed cell death and novel cancer therapies. He also relayed to the audience that passion, a focused research question and hard work are key ingredients to success.

Student presentations kick-started the student research symposium

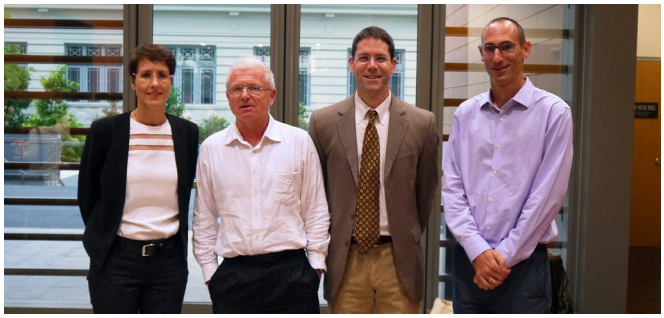


Poster showcase of student research projects

Students engaging in discussion with faculty members

In the afternoon, Dr. Kontos provided updates of his research centred on artery disease. Furthermore, in his capacity as the Director of the Medical Scientist Training Programme at Duke University, Dr. Kontos discussed and shared important issues with our MD/PhD students on how to succeed as a clinician scientist.

At the conclusion of the symposium, both Drs. Strasser and Kontos awarded students with plaques for best oral and poster presentations. Vera Goh and Veena Gopalakrishnan won prizes for the two best oral presentations. Best poster awards were given to Mohammad Idris, Bernice Wong, Melissa Wirawan, and Sheila Soh.



Keynote speakers Prof. Andreas Strasser (second from left) and Assoc. Prof. Chris Kontos, flanked by Assoc. Prof. Silke Vogel (left) and Assoc. Prof. David Silver

We rounded the day off with a new award - the most outstanding graduating student in the IBM PhD programme. This year, Eugenia Ong, was awarded this distinction for her thesis work and publications on dengue fever.

The Student Research Symposium has now become an important IBM tradition. Well done to all of our students, and we are looking forward to next year's event which promises to be another day of exciting research.

PROJECT DOVE: PAYING IT FORWARD

By Eshani Mathew

A team of 20 medical students and four doctors representing Project DOVE, the Duke-NUS Overseas Volunteering Expedition, organised annually by Duke-NUS medical students, had the privilege of travelling to Cambodia from April 26 to May 1 this year. In partnership with One-2-One Cambodia, an NGO based there, we cared for the underserved villagers in Kampong Spue province through a three-day mobile clinic and one-day health education programme.

After many months of planning, fund-raising and anticipation, we finally arrived in Phnom Penh on April 26, where the representatives of One-2-One Cambodia warmly welcomed us. We then travelled two hours by bus to Kampong Spue province.

At the crack of dawn, we started preparing for the first day of the health screening. Seeing the patient queue was undeniably intimidating, but every member of the team rose to the challenge. Our clinic ran from 8am until we attended to every patient who had travelled to see us. For three days, we manned triage, addressed their chief complaints, conducted physical examinations, presented our cases to the doctors-in-charge, and administered medication and counselling for a variety of complaints from musculoskeletal problems and fever to cough and abdominal pain. Though the inflow of patients seemed relentless, the Project DOVE team persevered and never turned a patient away. In total, we served nearly 450 patients.

School children at the Health Education Programme, with their group leader, Kenneth Chin (in black, last row)

Alicia Ong (left) and the local pastor (right) working at the mobile pharmacy

Min Kai Chang examining a patient at the mobile clinic

Eshani Mathew (right) triaging patients at the mobile clinic

One-2-One volunteers One-2-One volunteers Chanthorn (left) and Sandra Lynn educating a child on dental hygiene educating a child on dental hygiene

From left: Rayson Lee, Mervyn Chan and Dr. Courtney Davis, delousing school children during the health education programme

Despite the hot climate, intense working conditions and constant workload, we never felt more humbled and privileged to serve all those who came to us for help. None of this would be possible without the translators from One-2-One Cambodia who worked with our team tirelessly throughout the day and patiently translated our questions and instructions to all the patients.

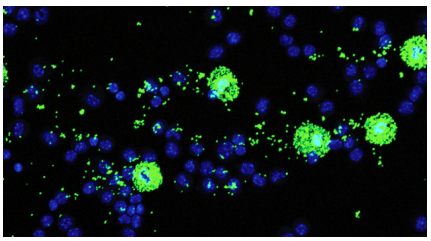
Our final day in Kampong Spue housed the health education programme for 470 students and six teachers. The students rotated through various stations, which included de-lousing, de-worming, nail clipping, dental health education and hand hygiene education. The local teachers attended a basic first aid workshop led by third-year Duke-NUS students that would enable them to educate teachers from other schools in the vicinity. Though we were honoured to provide medical interventions to the villagers in the previous days, we strongly believe that this health education programme would be a platform to make sustainable health and lifestyle changes.

This opportunity to take part in Project DOVE was an honour for every member of the team. It would not have been possible without the help of our sponsors and supporters. We would like to extend our thanks to the Vox Cordis Chorus, Lee Foundation, SingHealth, Narambi Café, NUS Faculty of Dentistry, Health Promotion Board, Aeras Medical Pte Ltd, and all the donors who contributed to our online campaign and donation jar. We learnt a great deal about medicine and ourselves, how to work with those from a different culture, express empathy through our actions, and to go the extra mile for our patients. Through Project DOVE, the motivation for entering the medical profession and wanting to serve others has been strongly reinforced for every member of the team.

Eshani Mathew is a first-year MD student from the Class of 2018. She was the Head of Publicity for Project DOVE 2015.

For more information on Project DOVE, please visit www.facebook.com/projectdovedukenus

Photos: Goh Kian Leong



UNCOVERED MECHANISM MAY HELP PREVENT SYMPTOMS OF SEVERE DENGUE

Assistant Professor Ashley St. John led research that discovered a new mechanism for mast cell activation during dengue infection. Mast cells are immune cells that communicate regularly with blood vessels. These findings provide new drug targets that might help alleviate the symptoms associated with severe dengue.

Dengue fever and more severe forms of dengue, known as dengue haemorrhagic fever and dengue shock syndrome, pose a burden in urban and sub-urban areas worldwide. When a patient is infected with one of the four distinct, but closely related serotypes (DENV-1, DENV-2, DENV-3 or DENV-4), that patient has lifelong immunity against that specific serotype. However, it is still possible for that patient to be infected with a secondary infection with one of the three other serotypes. Unfortunately, a secondary infection is a risk factor that could lead to more severe forms of dengue.

Dr. St. John and her team, from the Duke-NUS Emerging Infectious Diseases Programme, found that complexes of antibodies and dengue virus are able to bind to mast cells. This triggers the release of inflammatory products from the mast cells, which results in severe vascular leakage (image). This is a symptom of secondary dengue infection or severe forms of dengue and to a newly identified mechanism leading to severe dengue.

"Our research has revealed new stages in dengue infection that can potentially be targeted by drugs," explained Dr. St. John. "In future studies, we can test therapeutic agents that might reverse or stop patients from progressing from dengue into severe dengue, where no specific treatment or medicine is currently available."

Dr. St. John and her team also showed that mast cell stabilisers, were effective in blocking the enhanced vascular leakage that occurs during secondary dengue infection. Previous work from the group had suggested that mast cell stabilisers were able to treat primary dengue infection and their new data suggest that using these drugs in dengue patients may also be a potential way to halt the progression of dengue fever to severe dengue forms during secondary dengue infection. Dr. St. John, together with collaborators from the National University of Singapore and Singapore General Hospital, has launched a trial to test whether this strategy can limit vascular leakage in dengue patients.

The study was published in eLife and was supported by the Singapore National Research Foundation under its New Investigator Grant Programme and administered by the Singapore Ministry of Health's National Medical Research Council.

For more latest research news, please visit www.duke-nus.edu.sg/news

SOY DOES NOT INCREASE GOUT RISK

A study led by Professor Koh Woon Puay from Duke-NUS and Dr. Teng Gim Gee from the National University Hospital addresses that gap in research about diet and gout risk in Asian populations, showing that soy products and legumes are not associated with increased gout risk, contradicting popular belief.

Using data from the Singapore Chinese Health Study (SCHS), a longitudinal study of 63,257 Chinese adults aged 45 to 74 living in Singapore, Drs. Koh and Teng collected diet information at baseline and followed up for gout diagnosis for a period spanning 1993 to 2010. They then computed the association between different food sources of protein and incidence of gout. The results, published in *Arthritis and Rheumatology,* showed that eating more soy food and legumes was in fact associated with a reduced risk of gout.

Prof. Koh Woon Puay

Animal protein such as poultry, fish and shellfish was associated with an increased risk of gout, consistent with studies conducted in Western and Asian populations. "To our best knowledge, this is first prospective study to show that dietary intake of soy foods and legumes does not increase the risk of developing gout, and could even possibly be associated with a reduction in risk," said senior author Dr. Koh, who has a joint appointment with the Saw Swee Hock School of Public Health, National University of Singapore.

"Gout is due to high uric acid levels in the blood, and it seems intuitive to assume that any food that contains significant amount of purine, including meat, soy and legumes, should increase the risk of gout. However, our study suggests that plant-based foods such as soy and legumes do not increase the risk of gout, unlike animal-based foods such as meat. Hence, there is no need for patients with gout to worry about avoiding soy and legumes, especially since these foods have other health benefits against cardiovascular disease and cancer."

The SCHS is funded by grants from the U.S. National Institutes of Health, and receives active collaboration and support from the Singapore Ministry of Health.

TARGETING DENGUE THROUGH THE SKIN

Recent research by Duke-NUS Research Fellow Dr. Laura Rivino and Associate Professor Paul Macary from the Yong Loo Lin School of Medicine, National University of Singapore, provides insights into the workings of T lymphocytes (T-cells) and how they may be used to better target the dengue virus. T-cells are part of the body's immune response.

The team found that T-cells circulating in the blood of dengue-infected patients were capable of killing virus-infected cells. These dengue specific T-cells also had a molecule that drove their recruitment to the skin.

The results, published in *Science Translational Medicine,* support targeting T-cells to enhance their protective role against the dengue virus and implementing skin-directed immunosurveillance against dengue. It also suggests that a vaccine targeting the dengue-immune response could have protective effects.

This research was supported by the Singapore Ministry of Health's National Medical Research Council under its STAR Investigator Award, and the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme, administered by the Singapore Ministry of Health's National Medical Research Council.

For more latest research news, please visit www.duke-nus.edu.sg/news

IDENTIFYING GENETIC SIGNS OF CORONARY ARTERY DISEASE

Associate Professor Sujoy Ghosh from the Centre for Computational Biology at Duke-NUS has led a study that provides the most comprehensive list of biological processes that can lead to heart disease to date. Knowledge of these processes opens new possibilities for the discovery and development of medicines targeting heart disease.

Published in the journal *Arteriosclerosis, Thrombosis and Vascular Biology*, the study looked into the largest yet sample of coronary artery disease (CAD) patients and control subjects to identify genetic signatures of disease risk. Dr. Ghosh and his team used advanced bioinformatics and computational biology tools to identify key biological mechanisms that might be important for the development of CAD.

Using a systems biology approach, Dr. Ghosh and his team identified biological pathways that are associated with CAD due to enrichment in sequence variations in their constituent genes. Some of these genes are promising as potential targets for the development of new medicines. "Our large dataset and methodology made it possible to identify new pathways missed by earlier studies with smaller sample sizes," explained Dr. Ghosh, who is also from the Cardiovascular and Metabolic Diseases Programme at Duke-NUS.

Assoc. Prof. Sujoy Ghosh

"The uniqueness of this study is that we focused on understanding genetic susceptibilities at the level of biological processes and disease-associated functional networks whereas most other studies usually focus on single or a handful of genes at most. This approach allowed us to a more comprehensive understanding of the biological mechanisms disrupted in heart disease which can ultimately be helpful in improving patient care and the clinical management of heart disease."

The discoveries have the potential to affect all patients suffering from CAD or at a high risk for CAD. Although there are no immediate clinical or commercial applications of the research, the information generated will form the basis for follow-up studies to test novel therapeutic gene and pathway targets.

In future studies, Dr. Ghosh plans to test the genetic signals identified in this study for their value as predictive markers for risk of heart disease. This would lead to better population screening and prevention for CAD.

Research was supported with funding from the American Heart Association (AHA10SDG4230068) and the U.S. National Institutes of Health, (R21DK088319 and P20MD000175) and the Duke-NUS Signature Research Programme, with funding from the Singapore Ministry of Health.

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