# MediCine

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MALARIA FIGHTER, PRISONER OF WAR — NUS MEDICINE'S FIRST DEAN



Dear Friends,

Happy National Day! As the nation marks its 52nd birthday, the NUS medical school congratulates the new doctors and nurses from the NUS Class of 2017. We are confident that our new colleagues in Singapore's professional healthcare workforce will discharge their responsibilities and duties with unwavering professionalism, competence and compassion.

We also extend a very warm welcome to our incoming freshmen. Like their seniors, the Class of 2022 comprises young men and women who want to make a meaningful contribution to the health and well-being of Singaporeans. In addition to impressive academic results, these aspiring healthcare professionals are also blessed with skills and abilities and come from a varied background. Some also excel in sports, others during their national service. We have students who are gifted musicians, and others who are committed community service leaders.

NUS Medicine is also blessed with talented and experienced academic staff who inspire and motivate our students with their commitment to teaching and learning. Along the way, they make the School a vibrant and dynamic place for the exchange of ideas. That is why we are delighted to welcome Professor Brian K. Kennedy as a Distinguished Professor in the Departments of Biochemistry and Physiology and Director of the Centre for Healthy Ageing. Prof Kennedy's long and distinguished career in ageing research will enhance our work to understand the human ageing process and shed light on how to extend the period of healthy life or healthspan.

The focus on understanding the unique biology of human ageing in Singapore is driven by the dramatic demographic shifts in the Singaporean population, which is getting older at rates nearly unparalleled in the world. Ageing is recognised

as the biggest risk factor for a wide range of chronic diseases that are increasing healthcare costs and impairing life quality in elders. By understanding ageing and developing clinical interventions, it may be possible to extend human healthspan, the disease-free and functional part of life. Much thought and investment have been expended on efforts to improve the physical and social environment for the elderly in Singapore, though biomedical approaches leveraging on the latest scientific understanding of ageing have yet to be fully applied locally. We are therefore excited to have Prof Kennedy onboard at NUS Medicine and believe his expertise will provide critical direction and momentum for our healthspan research efforts.

NUS Medicine researchers are also at the forefront of work in synthetic biology, in which scientists manipulate genetic code and DNA to design and construct biological systems to improve existing functions or create new solutions to benefit people and the planet. You can read about this and other fascinating work in this issue of the newsletter.

Last but not least, we return to the early days of NUS Medicine during Singapore's colonial years and take a look at the life and times of the first dean of the School, Dr Desmond Faris. His story is told by his daughter, and it is a narrative that is at once absorbing and informative. This 112th year of the School, Dr Faris' dedication and service to those he served stand as a reminder of our enduring mission as Singapore's first medical school, one that was started by the community, for the community.

Happy reading.

Khay Guan

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and Assoc Prof Lau Tang Ching, Vice-Dean, Education (1st from right) with Class of 2017 Medicine students.

# MEDICAL DINNER 2017 REUNITES FRIENDS

They came from all over Singapore: teachers, tutors, mentors, collaborators, partners, alumni, staff, guests and this year's newly graduated Medicine, Nursing and Pharmacy students. More than 750 people gathered for an evening of fellowship and reminiscences at the Fairmont Hotel. It was also an evening to remember old friends for alumni from the Class of 1977 and 1967, who celebrated their 40th and 50th anniversaries respectively.

This year's theme paid tribute to the importance of teamwork in healthcare delivery, with professionals from different disciplines working together to deliver the highest quality of care to their patients. The theme was expressed by the combined efforts of students from Medicine, Nursing and Pharmacy, who worked closely to make the evening a thoroughly enjoyable occasion.

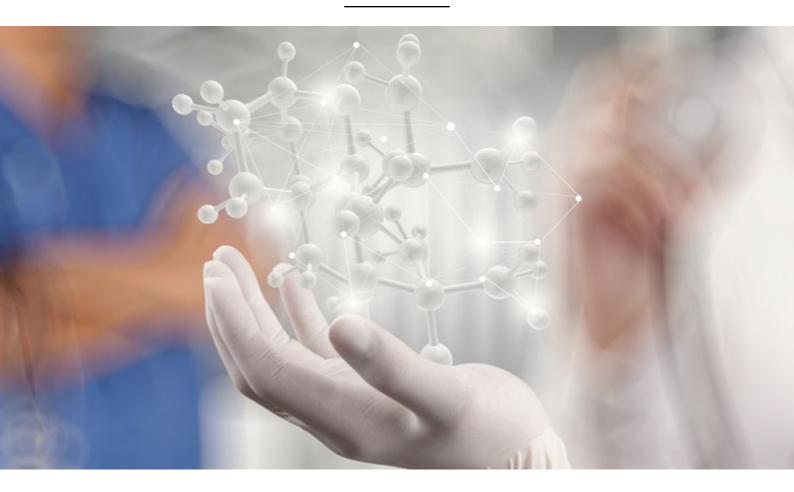












# MEDICAL SCIENCES CLUSTER AT NUS MEDICINE FORMED

The School has established a Medical Sciences Cluster comprising the Departments of Anatomy, Biochemistry, Microbiology & Immunology, Pharmacology and Physiology, effective June 1, 2017.

The aim is to build a stronger basic sciences identity and improve strategic coordination and synergies for research and education.

The Medical Sciences Cluster joins the family of clusters within the school and under NUH and NUS Medicine, namely the University Medicine Cluster, University Surgical Cluster, University Children's Medical Institute and the University Orthopaedics, Hand and Reconstructive Microsurgery Cluster. It is led by Professor Hooi Shing Chuan, Cluster Chair, Associate Professor Maxey Chung Ching Ming, Deputy Cluster Chair, and the respective Heads of the five Basic Science Departments of NUS Medicine.

Prof Hooi is well known in the community as having been the Vice-Dean for Education from 2010 till recently.





Left: Prof Hooi Shing Chuan; Right: Assoc Prof Maxey Chung

He joined NUS in 1985 and has held appointments including the Head, Department of Physiology from 2000 to 2008 and Assistant Dean (Pre-clinical Education) from 2009 to 2010. Since June 1, Associate Professor Lau Tang Ching has assumed the portfolio of the Vice-Dean for Education at NUS Medicine.

Assoc Prof Chung is the Deputy Head of Biochemistry Department at NUS Medicine. He has been with the Department of Biochemistry for more than 30 years and was the Acting Head, Department of Biochemistry from July 1, 2015 to March 31, 2016.



#### SAFE AND SOUND: THE QUEST FOR HEALTH AND WELL-BEING

The National University of Singapore and the National University Health System convened the inaugural Raffles Dialogue in 2015 as a gathering of global thought and opinion leaders to review the state of human well-being and security (HWS), a key concern facing all countries, rich and poor alike. The second Dialogue, takes place from September 4-6 this year. Prof Tikki Pangestu, Visiting Professor at the NUS Lee Kuan Yew School of Public Policy, and programme co-chairman for the 2nd Raffles Dialogue writes about the key issues to be discussed.

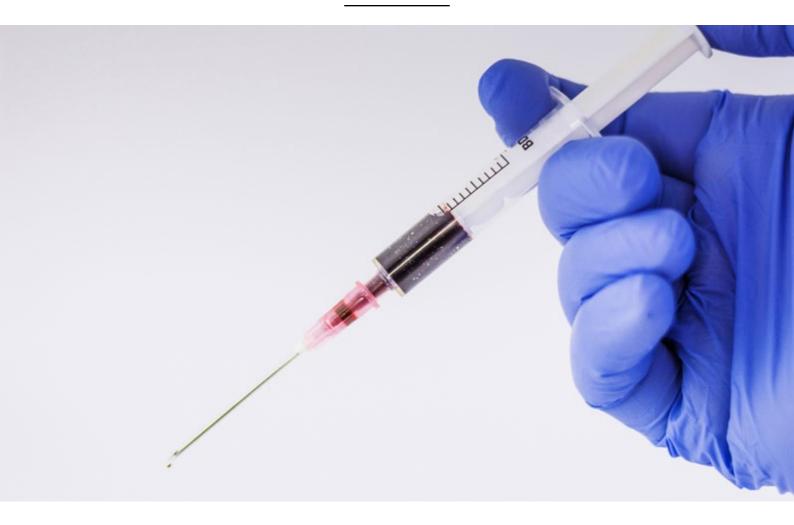
#### WHAT KIND OF A WORLD DO WE LIVE IN TODAY?

We live in a world dogged by instability, uncertainty and upheaval. Numerous threats to human well-being and security exist in the form of global warming and climate

change, often accompanied by extreme weather events which often result in natural disasters, famines and food insecurity. Epidemics of infectious diseases, antimicrobial resistance and chronic diseases continue to plaque the world, driven by the forces of globalisation, warmer temperatures, voluntary and forced movement of people around the world and the indiscriminate use of antibiotics. While globalisation has arguably lifted the living standards of many people and reduced global poverty rates, inequities continue to persist and many low- and middleincome countries still struggle with good governance and maintenance of peace, safety and stability for their populations. As populist and inward-looking sentiments dominate the world stage, international and multilateral organisations are under close scrutiny for being no longer 'fit for purpose' in an increasingly chaotic world.

#### HOW CAN HEALTHCARE PRACTITIONERS HELP TO ENSURE HUMAN WELL-BEING AND SECURITY?

Healthcare practitioners can continue to champion and promote all dimensions of human well-being and security. In its 1948 constitution, the WHO defined health as 'a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity'. In this regard, healthcare practitioners should focus not just on treating diseases but also on giving attention to preventive and rehabilitative strategies and promotion of health



more broadly, including mental and spiritual well-being. In this regard, and in the context of the increasing costs of healthcare globally, healthcare practitioners can play a crucial role in promoting healthy behaviours among the population. At the same time, healthcare practitioners cannot go it alone. In an increasingly inter-connected and inter-dependent world, they have to cooperate and coordinate closely with practitioners in other sectors of society, including those in the public sector and within communities and civil society.

#### WHAT SOLUTIONS WILL WORK?

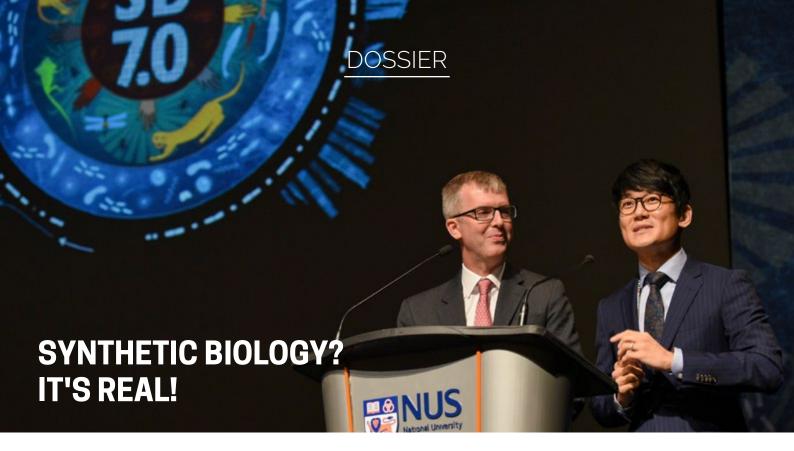
Rapid technology advances as a result of unprecedented advances in knowledge in the past century, especially in the life sciences, has resulted in many innovations which provide solutions in the areas of food security, curative and preventive medicine and epidemic preparedness which, collectively, may help to ensure the future of human wellbeing and security. These range from the development of pesticide-resistant crops with high nutritional value, to vaccines which prevent infectious diseases and cancer, and to rapid, accurate diagnostics to enable timely public health responses to disease outbreaks. At the same time, 'big data' analytics and powerful modelling tools are increasingly used to aid the development of better, evidence-informed policies in various sectors.

For these solutions to really work and have an impact,

however, they have first to reach those in most need. Equity, affordability and accessibility gaps still exist in ensuring that these solutions reach those in need, especially people living in the developing world. At the same time, technological solutions alone are insufficient — robust health systems founded on strong political will and commitment and societal acceptance are central to ensuring human well-being and security.

#### HOW RELEVANT IS THIS TOPIC FOR SINGAPORE, ASIA AND THE WORLD?

The topic is highly relevant for Singapore, which sees movement of humans and goods across its borders in large numbers, through trade, tourism and migrant workers. In a globalised world, and in a region still characterised by wide disparities in human and economic development, the topic is of great importance and relevance to Singapore. As a small, vulnerable island state, any upheavals or instability in neighbouring countries will directly affect and impact Singapore and its people. At the same time, Singapore, with its strong institutions and research capabilities, has much to offer the region and the world in terms of technical expertise and experience in various fields which will help to strengthen regional capabilities and preparedness in all dimensions of human well-being and security. In this way, Singapore has a key leadership role to play in the Asian region and beyond.



"If you think about the number of organisms on the planet, which may indeed exceed the number of stars in the universe, you'll realise that we're all running on the same software language," said Randal J Kirk, Chairman and CEO of synthetic biology company Intrexon Corp in his visionary lecture at the opening of The Seventh International Meeting on Synthetic Biology (SB7.0) on June 13 at the University Cultural Centre. This software language — DNA — is one of the main focuses of the meeting and the heart of the field itself.

Co-organised by NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI), the four-day conference brought together global practitioners of synthetic biology — academics, industry players, researchers and policy makers — to share, learn and debate on the latest efforts in the field, and to build partnerships and collaborations. Launched in 2004, the Synthetic Biology Conference series is the world's foremost professional meeting in the field.

As Guest-of-Honour Mr Desmond Lee, Minister in Prime Minister's Office and Second Minister for Home Affairs and National Development, aptly put in his opening speech, "The central idea of synthetic biology is that living cells can be programmed in much the same way we programme computers." Synthetic biology involves the manipulation of genetic code and DNA to design and construct biological systems with the aim of improving existing functions or creating new purposes. A rapidly advancing field, it is being used to transform and challenge various facets of the world today, including food, fuels, medicine and even in fashion.

This edition of the conference series was focused on three themes — "Revolution 2", "All People and the Planet", and "Diversity with Harmony", which aimed to get participants to discuss the next technical and scientific step in the field and address possible implications on the planet in an inclusive environment of openness and sharing.

SB7.0 WILL PROVIDE A UNIQUE PLATFORM FOR A GLOBAL COMMUNITY OF SYNTHETIC BIOLOGISTS TO GATHER AND PLAN TOGETHER FOR COLLECTIVE GROWTH OF OUR SCIENCE, ITS BENEFICIAL APPLICATIONS. AND RESPONSIBLE PRACTICES.

Assoc Prof Matthew Chang (right)

"Biology is central to all of human existence and nature. While synthetic biology is already being used to advance many aspects of our life, to ensure that synthetic biology can benefit all people and the planet, I believe the international synthetic biology communities must work together. SB7.0 will provide a unique platform for a global community of synthetic biologists to gather and plan together for collective growth of our science, its beneficial applications, and responsible practices," said Associate Professor Matthew Chang, from NUS Yong Loo Lin School of Medicine and Director of SynCTI and the Singapore Consortium for Synthetic Biology (SINERGY). He co-chaired SB7.0 with Associate Professor Drew Endy from Stanford University.

The conference featured more than 100 speakers in 12 thematic sessions. Topics shared included research into restoring extinct and endangered species, storing media in DNA and using yeast to produce painkillers, as well as broader topics addressing the future of synthetic biology, leadership development and the challenges the field may face.

Over 40 countries were represented in the 900 participants in the conference. Three hundred students, researchers and leaders from local tertiary institutions also attended the event.

This article was first published on June 15, 2017 in NUS News at http://news.nus.edu.sg/highlights/advancing-synthetic-biology



#### By Dr Khor Ing Wei, Department of Medicine

While watching the documentary "Cooked" on Netflix recently, I was captivated by the part where writer Michael Pollan talks about eating a wedge of cheese grown with special bacteria and getting protected from disease. Wow! Visions of being vaccinated with Parmesan shavings popped into my mind. The truth is that we aren't far from the day when these scenarios could become reality, and the research to make it so is happening right here at NUS Medicine.

Applying design and production principles from synthetic biology, Associate Professor Matthew Chang from the Department of Biochemistry and the NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI) is leading a new research programme to modify microbial genes to produce safe and effective therapies for a range of important diseases. The programme is one of the NUHS's Summit Research Programmes, which bring together basic and clinician scientists from different disciplines to drive academic excellence, accelerate research outcomes, and train new clinician scientists.

The microbes in question are the 10 to 100 trillion bacteria and yeasts living in our bodies (mostly in the gut), which together comprise the microbiota.¹ Put together all of the genes of these trillions of organisms and you get the microbiome. The SRP team is figuring out the role of the microbiota and microbiome in infectious disease, metabolic disease and cancer, as well as tweaking some of our gut bacteria to create therapies for these diseases. Such engineered bacteria lend themselves well to oral therapies since they thrive in the gut environment. They also stay in

the body for a long time, thus could be taken less frequently. However, long-term safety becomes very important — this could be ensured by measures such as changing the genes that control the production of toxic substances.

#### **ENGINEERED MICROBES IN INFECTIOUS DISEASE**

Pseudomonas bacteria are a major cause of hospital-acquired infections such as respiratory infections that start in the gut. The worrying thing about these infections is that they tend to be resistant to multiple antibiotics, which leads to a high rate of mortality from the bacteria in the blood and all over the body (sepsis). Dr In-Young Hwang, lead of the Mammalian Synthetic Biology progamme and co-lead of the Therapeutic Cell programme in Assoc Prof Chang's lab, headed the work in engineering "good" E. coli bacteria to sense and kill the harmful Pseudomonas bacteria. In animals, the engineered bacteria could clear established infections as well as prevent infections from gaining a foothold.<sup>2</sup>

The advantages of this system are: 1) its specificity - the engineered bacteria only release their toxins when they detect *Pseudomonas* bacteria in the vicinity; and 2) its ability to break down and prevent new biofilms, which are layers of bacteria within which the bacteria can hide from the action of antibiotics.

The team, which includes clinician scientists Dr David Ong and Dr Louis Chai, is also targeting *Clostridium difficile* bacteria, which also have a strong tendency to become antibiotic resistant, to make them more susceptible to the drugs. Engineered bacteria thus represent a novel addition to the limited treatment options for multidrug-resistant bacterial infections.

#### **ENGINEERED MICROBES IN METABOLIC DISEASE**

Assoc Prof Chang is working with clinicians Associate Professor Lee Yung Seng, Associate Professor Dan Yock Young, Dr Yvonne Lim, Dr James Huang and Dr Jonathan Lee to identify the types of bacteria that are associated with good health, eg, low risk of obesity and diabetes, as well as bacteria that are linked to undesirable conditions. Once these health-promoting bacteria are identified, the team aims to selectively enrich such bacteria through successive life cycles, and pinpoint the proteins responsible for these beneficial effects. The researchers can also engineer other microbes, such as "good" E. coli, to produce these particular proteins. Eventually, people could just consume the engineered microbes in the form of a pill (or a piece of cheese!) The microbes would make their way to the gut without much digestion by stomach acid, and enhance the production of favourable hormones and control glucose absorption.

The team is now identifying bacteria in the gut that are linked to good metabolic health. Previous studies found that favourable microbiota are specific to populations. For example, microbiota that have been linked to good metabolic health in Western populations are not beneficial in Asian populations. Profs Lee and Sanjay Swarup at the Singapore Institute of Clinical Studies (SICS) and Singapore Centre on Environmental Life Sciences Engineering (SCELSE) respectively, are studying the insulin responses and stool microbiota of 25 Indian, 25 Chinese and 25 Malay young men, after consumption of different types of food. The work is still in progress, but ethnic differences are emerging in the types of bacteria that are important for metabolising specific foods.

#### **ENGINEERED MICROBES IN CANCER**

Despite significant advances in cancer treatment during this period, current therapies still come with a range of side effects such as nausea and low blood cell counts. Another problem is the inability of cancer therapies to completely eliminate cancer cells, which can result in cancer recurrence and a high risk of death. To help overcome these issues, researchers are exploring new treatment options, one of which is the use of engineered microbes. Although the idea of using bacteria to fight cancer has been around for more than a century, the advent of synthetic biology is now making it a reality.

Using bacteria to fight cancer is appealing for several reasons. Firstly, cancer cells produce substances that suppress the immune response, creating a friendly environment for bacteria to grow. Secondly, many solid tumours are oxygen deprived, which certain bacteria called anaerobic bacteria actually prefer. Some of these anaerobic bacteria multiply better in solid tumours than in healthy tissue, giving them an inbuilt specificity for tumor tissue.

For example, researchers have engineered Bifidobacterium bacteria (a common probiotic supplement) to express anticancer substances such as the thymidine kinase enzyme produced by the Herpes simplex virus. Thymidine kinase converts a compound called ganciclovir into a toxic





Left: Dr Chun-Loong Ho; Right: Dr In-Young Hwang

substance that kills the tumours.<sup>3</sup> Even the much maligned *Salmonella* bacteria can be used to detect tumors or to destroy them by delivering a payload of cancer-killing substances. These *Salmonella* organisms are either harmless strains or altered bacteria that do not cause food poisoning. Engineered probiotics have been shown to be effective against a range of cancer types, including cancers of the colon, liver, stomach, breast and skin.

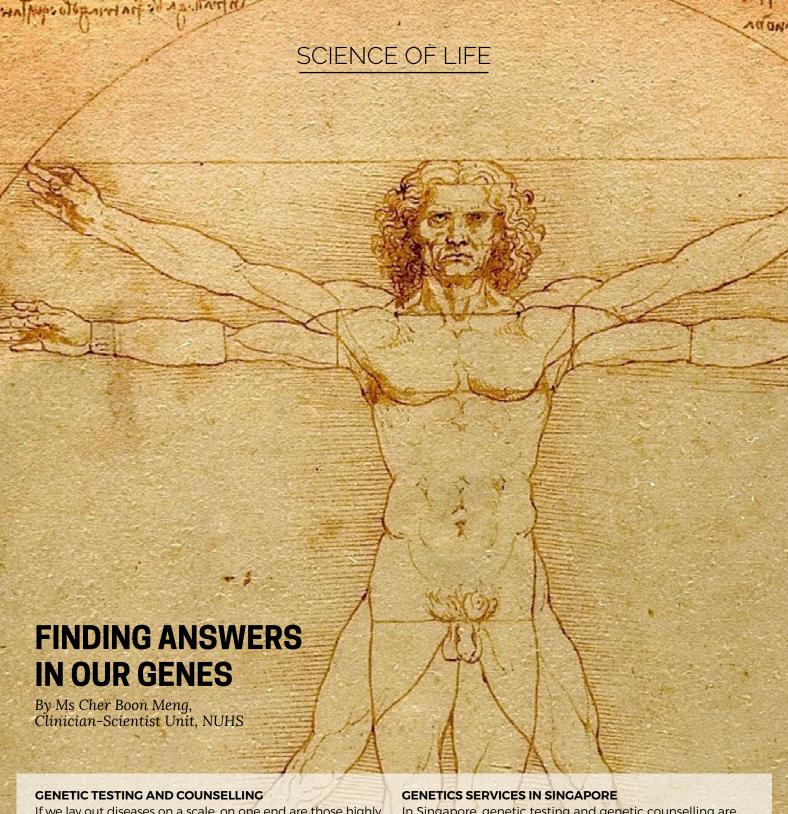
Dr Chun-Loong Ho, who co-leads the Therapeutic Cell programme in Assoc Prof Chang's lab, is engineering probiotics to specifically target colorectal cancer cells. They engineered E. coli Nissle to be a probiotic that attaches to the surface of colorectal cancer cells and secretes an enzyme that converts dietary substances found in vegetables into anticancer agents. The engineered probiotics plus a vegetable extract result in the killing of more than 95% of the cancer cells in a dish. In mice with colorectal cancer, the engineered probiotics caused, on average, a threequarter reduction in the number of tumours and a 3-fold decrease in tumour size than in untreated mice. He and Dr Yong Wei Peng, a colon cancer specialist, envision using these probiotics as tools to help clean up the cancer cells remaining after the larger tumors have been surgically removed. They are also working on converting waste substances into anti-tumour agents.

#### **TESTING THEM IN HUMANS**

So far, most of the infectious disease and cancer research has been in animals, but the team plans to test the more promising therapies in humans soon. As Prof Lee says, "The strength of the SRP is that it involves both scientists and clinicians from the beginning. Unlike most clinical and basic science collaborations, the clinicians in this programme feel that they have ownership and can shape the experiments from an early stage, based on their clinical knowledge. The scientists have the know-how to make it work."

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If we lay out diseases on a scale, on one end are those highly influenced by environmental and lifestyle factors. At the other end are diseases with far stronger genetic contribution, which include Huntington disease, haemophilia, and Marfan syndrome. Some diseases are clearly linked to a specific genetic variant, which genetic testing can help uncover. Testing tells whether an individual has the specific genetic variant and is thus predisposed to develop the disease. Genetic counselling, performed both pre- and post-test, guides patients on understanding their risks and to consider their next step — how likely the disease will occur, should genetic testing be done, and how to mitigate severity when the disease strikes.

In Singapore, genetic testing and genetic counselling are overseen by clinical geneticists (doctors who have subspecialised in genetics) or other subspecialists trained in the genetics of a particular disease. Often, clinical geneticists work with genetic counsellors when providing counselling to patients.

"We can classify test takers roughly into two groups," says Associate Professor Roger Foo, Cardiac Department, National University Heart Centre, Singapore (NUHCS). "Those who test for a medical reason, and those who test just out of curiosity".

In Singapore, most of the patients seen by a clinical geneticist or genetic counsellor fall into the first group.

Assoc Prof Foo and genetic counsellor, Ms Yasmin Bylstra, work with patients who have inherited cardiac conditions such as cardiomyopathies, connective tissue disorders, and arrhythmias. At the National University Cancer Institute, Singapore (NCIS), Associate Professor Lee Soo Chin heads the Cancer Risk Assessment and Genetics Clinic, which offers testing for BRCA1/2 mutations and cancer syndromes such as Lynch syndrome. Meanwhile, Associate Professor Denise Goh Li Meng, Department of Paediatrics, NUH, offers testing for many genetic conditions. She sees a wide range of patients, from couples planning to start a family to newborns and adults.

For the second group, ie those who text to satisfy their curiosity, Direct-to-Consumer (DTC) tests are popular. These are tests that are available to the public and do not require consultations with doctors. Some tests provide information on genetic health risks, while others tell consumers their ancestry. The appeal of these tests lies in their convenience, relative affordability, and non-invasiveness. Consumers order a kit, provide a saliva sample, and mail it back to the genetic testing company. In due course, customer receives a genetic profile report. However, DTC tests come with their own set of issues (see Facts Box). In Singapore, DTC genetic tests are strongly discouraged.

#### A GENETIC COUNSELLING SESSION

During the session, the genetic professional will learn about the patient's family history. Typically, a patient provides notable medical histories of at least three generations of his or her extended family, which includes grandparents, aunts, uncles, and first cousins. Information on diseases and test results will also be gathered. Besides information on inherited disorders, the genetic professional will also learn about the patient's lifestyle, diet, other environmental exposures, and medications.

Genetic counselling involves not just scientific explanations of risks, probabilities and disease courses; it also includes a psychological component, offering psychosocial support, and helping patients cope with their situation. Pre-test, genetic professionals help patients understand testing options and implications of testing, to ensure informed consent. Post-test, genetic professionals help patients navigate the array of steps they can take based on their genetic profiles, and provide a roadmap showing the implications of each option. These options may include lifestyle modifications, reproductive planning, palliation, and more. The genetic professional may also make healthcare recommendations for at-risk family members or offer testing. Importantly, rather than prescribe a course of action, the genetic counselling session provides the patient with the relevant information to make a decision about testing or treatment and how to communicate information about their genetic condition to at-risk family members. Unlike typical doctors' visits, genetic counselling sessions are longer and can last up to 45 minutes or an hour.

Assoc Prof Denise Goh cautions that genetic tests and results are complex, and understanding and

communicating them requires specialised domain knowledge. No test is perfect and a trained professional is better able to differentiate false negatives from true negatives, and false positives from true positives when interpreting results. They are able to tell if a particular variant is pathological, benign, or has unknown significance. Even if a pathological variant exists, a genetic condition may not have a 100% evolution rate. One example is BRCA1/2 mutations, where not all carriers will go on to develop breast cancer.

#### **ETHICAL ISSUES**

Although anyone can request for genetic testing, Assoc Prof Roger Foo recommends having very clear reasons for doing so. The knowledge that one carries a pathological variant may be burdensome or even traumatic for some. Thus, the decision to test should not be taken lightly.

The results from genetic testing are permanent, out-living the individual. As such, testing may have implications for insurability and employability. Although insurance agencies and employers do not have the right to access an individual's genetic information, they can request applicants to declare any genetic information, increasing the risk of genetic discrimination.

Another ethical issue centres round underage, asymptomatic patients whose parents want them to be tested for genetic conditions that manifest later in life and for which no early intervention is available. Testing thus takes away these children's right to make informed decisions in the future. Current guidelines state that for such patients, testing should be delayed until these children reaches adulthood and can make their own decisions.

The privacy of genetic information concerns not only the individual, but their relatives as well. Due to a shared genetic heritage, genetic testing of one individual may reveal information about a relative, such as a parent, regardless of that relative's wishes.

Another ethical issue is that of incidental findings, where mutations unrelated to the patient's symptoms are picked up during a test. It is not possible to "un-know" a piece of information, although Ms Yasmin Bylstra explains that patients can make the choice whether to receive incidental findings. Incidental findings also come with a whole host of ethical considerations, which have been extensively debated.<sup>1</sup>

Some experts hold the view that knowing may be pointless if there is no treatment (termed medically non-actionable). To this, Assoc Prof Goh posits the concept of utility to patients, which is distinct from medical actionablility. Whether or not a treatment or cure exists, knowledge about their risk for a disease allows the patient to plan for the future and make necessary adjustments.

#### CONCLUSION

Genetic testing can reveal useful information regarding health risks, allowing us to prepare for what may come. However, it is not an unmitigated good; risks to genetic testing exist and need to be weighed against any benefits. Given the bewildering amount of technical information produced by a genetic test, geneticists and genetic counsellors are invaluable in helping patients make sense of the data and find their way to a decision.

#### **Facts Box:**

#### Drawbacks of Direct-to-Consumer (DTC) Genetic Tests

In their 2005 guidelines, the Bioethics Advisory Committee of Singapore strongly discourages the use of DTC tests<sup>2</sup> due to several ethical concerns.

#### **Uncertain quality:**

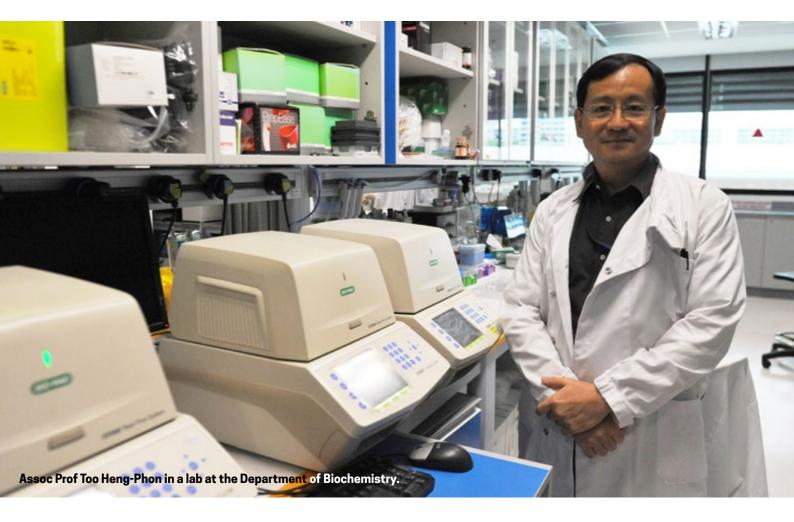
- For disease risk: only one has been FDA-approved --23andMe Personal Genome Service Genetic Health Risk.
- 23andMe has a history of selling DTC tests without FDA approval, despite attempts by the FDA to help the company comply with regulations. In 2013, the FDA issued a warning letter<sup>3</sup> to stop marketing of the test.
- Although consumers are provided with information to help interpret their disease risk, inaccuracies or misunderstanding can arise without consultation with genetic professionals.
- For ancestry testing, heritage results differ among companies, depending on the sample database, how regions are divided, and how many genetic markers are used.

#### Genetic information privacy:

 Some providers have questionable privacy terms, eg, AncestryDNA™'s policy states that it can use genetic information in perpetuity, royalty-free. These uses could include providing information to insurers, employers, and law enforcement agencies.

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## THE WARRIOR'S WAY TO BIOTECH SUCCESS

By Dr Khor Ing Wei, Department of Medicine

What does it take to nurture a biotech startup into an enterprise that is worth millions?

Patience and perseverance. And a good healthy dose of martial arts zen, according to Associate Professor Too Heng-Phon. "In karate, there is no first strike, but when you strike, you strike to kill. You wait for the right time, and you whack the guy once, that's enough. So it's the same thing when you want to do something right, go for the kill."

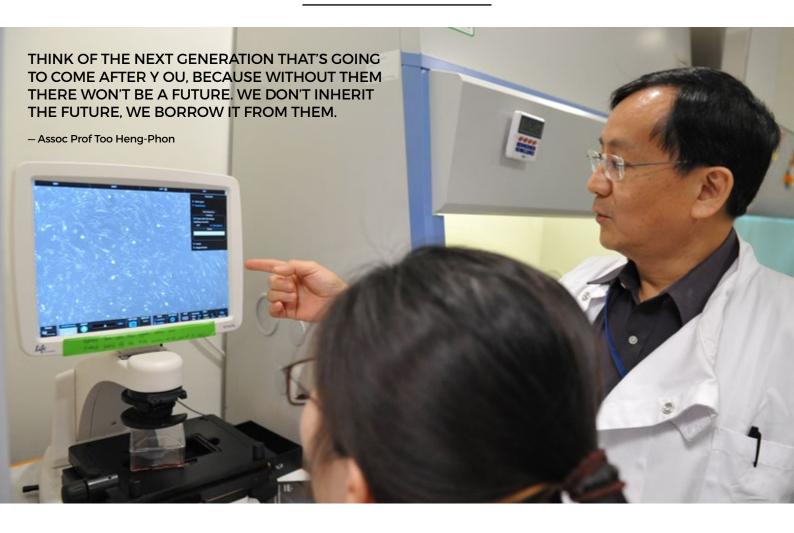
The man knows what he is talking about. The second dan karate black belter has plenty of scars from the long years of struggle, fighting to turn decades of scientific research into an extremely successful and uniquely Singaporean biomedical company. The firm, MiRXES, now employs more than 20 people and has also established a presence in China and in Harvard.

#### **MEASURING MICRORNA IN BLOOD**

In the 1990s, Assoc Prof Too started studying short segments of non-coding RNAs called microRNAs. Although made

inside the cell, microRNAs can also be found outside the cell, in the blood. By affecting the expression of different genes, microRNAs is known to influence a wide range of biological functions, including the process by which normal cells change into cancer cells. Then, researchers started noticing that certain patterns of microRNAs in the blood corresponded to cancer (the levels of some microRNAs are consistently elevated, while others are consistently reduced), suggesting that measuring microRNAs could be a non-invasive alternative for detecting early cancer — a form of liquid biopsy. Surprisingly, given the notoriously unstable nature of RNA, these microRNAs are very stable in blood.

However, all was not smooth sailing. The methods that were being used to detect microRNAs in the blood were inconsistent and performed poorly. Assoc Prof Too and several of his PhD students at NUS Medicine's Department of Biochemistry decided to develop a method to detect these microRNA patterns. After exploring different methods, they chose quantitative polymerase chain reaction (PCR) as the platform, which is a way to amplify and measure the amount of genetic material in a sample. Assoc Prof Too's team proceeded to develop a method and with computational algorithms to analyse the large amount of microRNA data coming out of the PCR experiments.



"I am very stubborn. If I want to build something, by hook or by crook, I am going to make it work. And if it fails, then at least I've tried."

#### FRESH HURDLES AND BIRTH OF MIRXES

After developing a robust method that consistently performed well and then moving to venture into biomarker discovery, they realised that there was a need to set up a company to perform the assays and face the real world. That was where they ran into a fresh set of problems, and which would trouble the team for a number of years.

These would see Assoc Prof Too not being able to secure funding from any organisation to develop the technology further. At the nadir of his anguish, he was almost ready to leave Singapore for Hong Kong. But then funding finally came in one night in 2010. Exploit Technologies Pte Ltd (ETPL) at A\*STAR agreed to fund the proof-of-concept for commercialisation for one year, and Assoc Prof Too was able to translate his research into a start-up company, MiRXES.

MiRXES produces diagnostic kits that can help doctors accurately detect, with a few drops of blood, whether a patient has developed gastric, breast, colorectal or lung cancer. This kit detects the patterns of microRNA — a type of gene — in a blood sample, and the results can be obtained within three hours.

The technology is beginning to be adopted in hospitals beyond our shores, Assoc Prof Too's team is working with the Health Sciences Authority's regulatory board to pave the way for the diagnostic kits to be used in local hospitals.

MiRXES was established by Assoc Prof Too and three of his PhD students. Today, they run the multimillion-dollar operation together with Assoc Prof Too, who works as a non-executive director to the local biotechnology start-up. MiRXES has also expanded from a four-man team, to a team of more than 30 employees globally.

#### **LEGACY AND VALUE CREATION**

The teacher strongly believes in paving the way for the future generation.

"I share all my stuff with my students. Think of it, why do I need all these? I have already made it, so why bother? If the professors don't help the next generation, how are they going to start rising? Somebody has to give them a start. My professors, my mentors, gave me a start. So similarly, everybody in the university should think that way. Think of the next generation that's going to come after you, because without them there won't be a future. We don't inherit the future, we borrow it from them (the next generation)."

MiRXES has also ventured into Hangzhou, China, where



Assoc Prof Too intends to recruit more staff to form a team of 30, up from the current team of eight staff members. His team is also working with Zhejiang Cancer Hospital on research into lung cancer.

"Hiring them (the Chinese) is easy, and they know much more than us. They work with China Food and Drug Administration, and the market there is huge. Those guys have an "everything can-do" attitude," he says.

At the end of last year, MiRXES was named the "most promising start-up" in the Emerging Enterprise Award 2016. Success has brought suitors in the form of companies expressing interest to invest or buy stakes in the firm, whose difficult genesis is something its founder remembers and even celebrates.

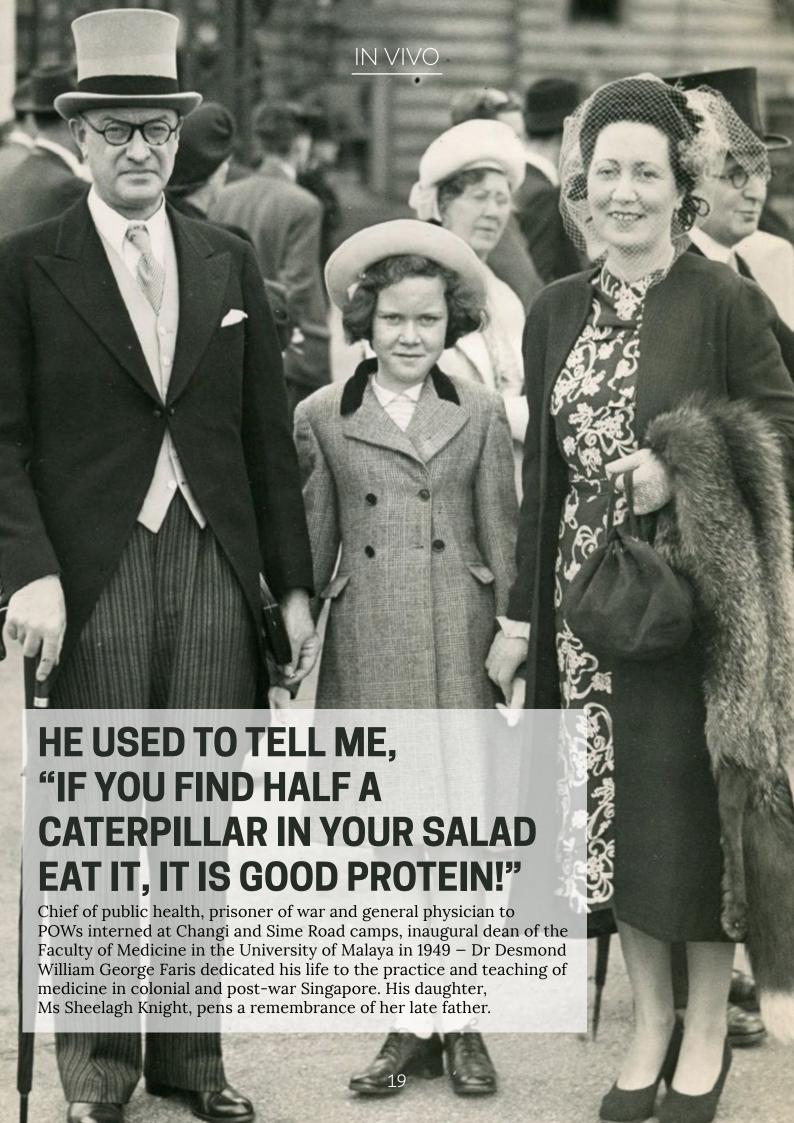
The 'S' in the MiRXES stands for Singapore, he says, illustrating the importance of situating the company and performing the bulk of the work in Singapore, instead of selling the license to other companies for profit like many start-ups do.

"It is an easy way out for start-ups to give it away, to incubators, businessmen and multinational companies. But if you ever do that, you can never create value for Singapore." "The key reasons to set up a spin-off company are to save lives and to contribute to the ecosystem. Another reason for establishing a spin-off is to obtain funding beyond money coming in from grants, which is very unpredictable in Singapore." However, setting up a company based on original research should "never be about making money" because, if such companies do one day produce a return on the money invested, that day could be a long time in the future. Beyond the possibility of turning a profit, Assoc Prof Too feels that spin-off companies are an important part of promoting innovation in Singapore and building a vibrant biotech culture here.

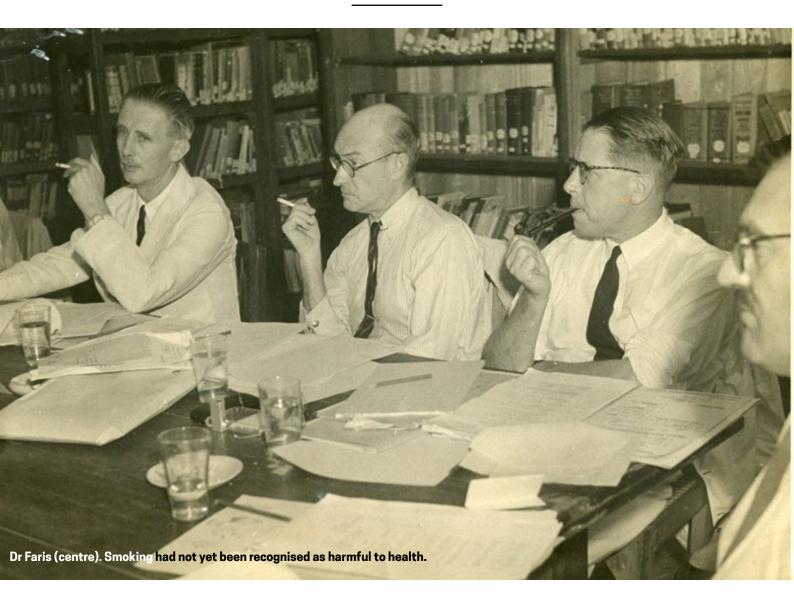
#### KARATE'S PHILOSOPHY

Back to the karate: outside of his teaching and research work, Assoc Prof Too dedicates three days each week to practising and teaching karate to both children and adults. He is also the vice-president of the Ken Yu Kai Karate Association Singapore.

"I practice karate for its philosophy. It is very important, every time you go into a karate class, you are humbled as you know that there are others better than you. In 'kumite', you block, you try to evade the onslaught of punches and kicks. This philosophy to me is very nice, and there is a deeper meaning to karate, it is how the underdogs can learn and rise to the top."



#### IN VIVO



Desmond William George Faris was born in Ennis, County Clare, Southern Ireland (Eire) on April 30, 1901. His father was a doctor and his mother a nurse. The family moved to England in the early 1910s and Desmond was educated at Epsom College. He received his medical training at what was then the London Hospital and thereafter at the London School of Tropical Medicine.

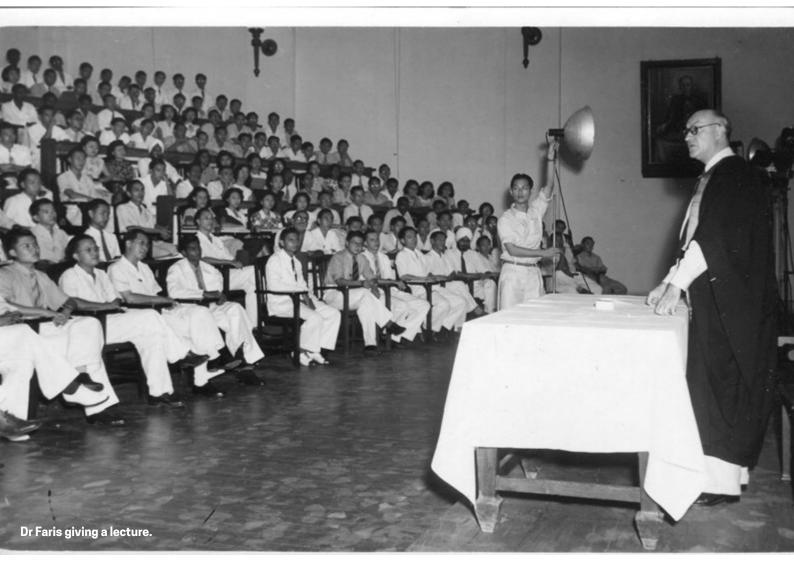
Upon receiving his professional qualifications, he joined the Medical Colonial Service and went to Malaya. He worked 'up country' with Dr William Oscar Pou, where they were particularly concerned with the eradication of malaria. He married Doctor Pou's daughter Olive on March 29, 1930. They lived and worked in various parts of Malaya before moving to Singapore.

He was part of the Public Health Department in Singapore and was soon appointed Chief Health Officer. He was head of Public Health when the war came to Malaya. My brother had been born in Klang in 1932 and was sent back to England to school. I was born in Singapore in the General Hospital in 1937. I remember as a 'bad dream',

a Japanese bomb going through the roof of our house — fortunately, it did not explode. As the Japanese advanced on Singapore, my father felt it was his duty to remain, in order to maintain as high a standard of public health as might be possible. He was, however able to secure passage for my mother and me to Australia.

He was interned by the Japanese, first in Changi Prison and then later, as that became a camp only for the military, at the Sime Road Camp for civilians. Whilst he was in Changi Prison, the frame of his spectacles unfortunately broke; it was skilfully repaired by another internee using a discarded toothbrush. (The repaired frame was to last until after his liberation!)

In Sime Road Camp, he came to be in charge of the health of the internees, and it was largely because of his insistence on cleanliness and a healthy diet that so relatively few people died there. He used to tell me, "If you find half a caterpillar in your salad eat it, it is good protein!" Towards the end of the war, my father and his team started harvesting snails to provide extra protein for



the internees. He was later awarded Commander of the Most Excellent Order of the British Empire (CBE) for services during his internment.

The camp was finally liberated in 1945. My mother was most upset that he did not come back to the UK immediately; he insisted on remaining in Singapore for as long as it took to make sure his fellow internees were suitably cared for.

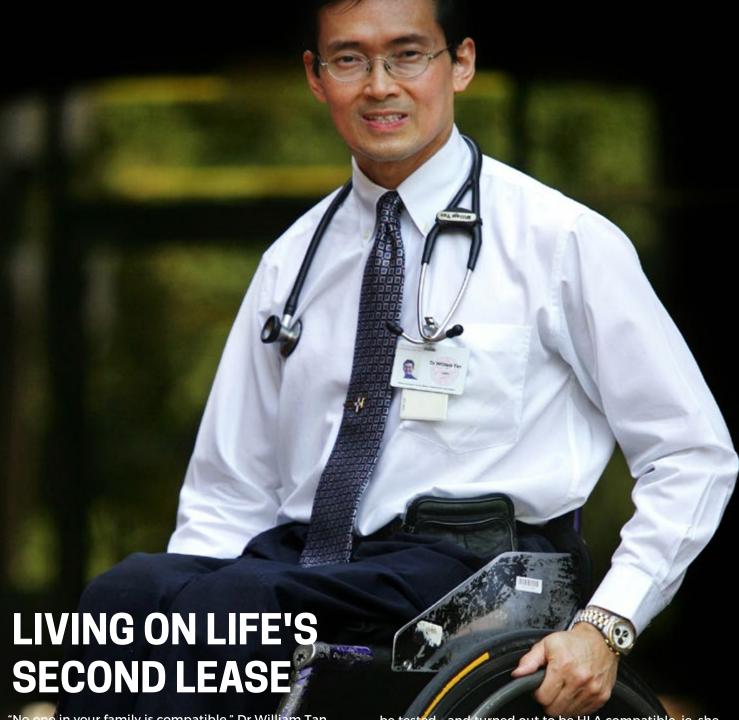
In 1946 however, he was asked to return to Singapore to become the Principal of the King Edward VII College of Medicine. He helped with the decision to merge that College with Raffles College, and that it should then become the University of Malaya, which happened in 1949. He then became the first Dean of the Faculty of Medicine, a post which he felt honoured to take on. However, as the University was new, there were many tasks that had to be sorted through. He always paid great attention to detail and was constantly concerned that he had got the right answers. Both he and my mother were very good at entertaining the various dignitaries that used to

visit. My mother was also very involved with the St John's Ambulance Brigade in Singapore.

My parents returned to England in 1955 upon my father's retirement. He was delighted to have had a lecture hall in the Faculty named after him, as he was also to receive an Honorary Doctorate of Laws from the University. Sadly, he died of a coronary thrombosis on March 20, 1957 before he and my mother could really enjoy retirement. My last memory of him is saying goodbye on the station platform as I returned to London, and him telling me how difficult it was to talk about his wartime experiences, except with those who had also survived them.

On Tuesday, November 2, 2016 my daughter Catharine and her husband Nick Brode were warmly welcomed to the Faculty of Medicine (now known as the NUS Yong Loo Lin School of Medicine) on a short visit. Both they and I would like to express our profound appreciation for the honour and courtesy extended to them as descendants of my father, Dr Faris, by all their hosts from the School that day.

#### WITH A LITTLE HELP



"No one in your family is compatible." Dr William Tan vividly recalls hearing these words from his oncologist after his siblings had been tested as potential bone marrow donors. The long-time donor to NUS Medicine had undergone several bouts of chemotherapy for his Stage four chronic lymphocytic leukaemia, and now needed a bone marrow transplant. The words hit him like physical blows to the gut. However, after the initial shock, he realised that they were not strictly true because not all of his siblings had been tested. Susie, the second eldest sister among Dr Tan's five siblings, had been his arch nemesis growing up and the two had fought often. Also, she was very thin, so appeared not to be a good prospect. Finally, after some deliberation, Dr Tan called his sister and explained the situation. She immediately agreed to

be tested - and turned out to be HLA compatible, ie, she and her brother shared the same type of HLA protein on their cells, indicating that he could receive some of her cells with less risk of rejection by his immune system. The outcome of this dramatic turn of events was a successful transplant on Children's Day (October 1) of 2009. Dr Tan joked that this was fitting because he felt like "a newborn child."

#### Birth of a wheelchair athlete

Dr Tan's successful transplant was just another challenge that he had overcome. Like too many Singaporean children in the 1950s and 1960s, he had not been vaccinated against polio because of the inconsistency of childhood vaccinations in Singapore at the time.

#### WITH A LITTLE HELP



A bout of polio had then consigned him to a wheelchair for life. Undeterred, Dr Tan became a Paralympic wheelchair athlete, specializing in sprints, marathons and ultramarathons (any race longer than the marathon distance of 42 km). It was through his ultramarathons that he raised donations for several professorships at NUS Medicine, including the Parkway Professorship in Geriatrics, Chao Tze Cheng Professorship in Forensic Pathology, and the Viva-Goh Professorship in Paediatric Oncology.

#### The path to medical school

After his application to read Medicine at the University of Singapore (as NUS was then known) was not accepted, he completed a Bachelor's in Science, followed by a Masters in Physiology and a PhD in Neuroscience. However, while a neurosurgical research fellow at the Mayo Clinic in the United States, he was inspired by a wheelchair-bound Chief of Neurology to rekindle his dream of becoming a doctor. Although he initially intended to apply to U.S. medical schools, he changed his mind upon talking to a visiting Australian neurosurgeon. After applying and receiving offers from a few Australian medical schools, Dr Tan chose the University of Newcastle because of its unusual self-directed, problem-based teaching approach, which included the opportunity to interact with patients early in the medical course.

Even after completing medical school and housemanship,

Dr Tan's plans for a career in rehabilitation medicine were forever altered by a series of unexpected events. Firstly, on December 1, 2006, former Ambassador-at-Large Professor Tommy Koh asked Dr Tan to return to Singapore, in part to champion the cause of the disabled. Dr Tan could not resist the opportunity to contribute to Singapore as a doctor and was all set to move back home and take up a post asa resident physician at the National Cancer Centre Singapore (NCCS).

What happened next not only changed Dr Tan's career, it turned his life upside down. He had continued to compete in marathons over the years and decided to attempt the Paris marathon before taking on his new role at NCCS. However, during the marathon, he started bleeding profusely.

On his return to Singapore, the doctors gave him a daunting diagnosis: Stage 4 chronic lymphocytic leukaemia. He went through a period of disbelief and depression. From being a doctor with a promising future ahead of him back in his home country, he was now a cancer patient, and a very sick one at that. Everything came home to him at once. How he had struggled and persevered for so many years to qualify as a doctor, then the diagnosis of cancer just as he was about to embark on his long-cherished dream of becoming a doctor in Singapore. How his type of leukaemia was extremely



rare in Asians and in adults younger than 55, but he just happened to have a mutation in his genes that caused him to have abnormally low levels of P53, a protein that protects against many types of cancer. Against the odds, chronic lymphocytic leukaemia was now part of his reality — how did he get to be so "lucky"?

#### His dark night of the soul

A bleak period followed when the doctors tried out different treatment protocols for his leukaemia. They started him on the drug rituximab, but the first injection sent him into anaphylactic shock, causing his blood pressure to plummet and almost killing him. To tame his allergic response, his doctors switched from injecting the drug to slowly infusing it, and also gave him steroids. This helped with the side effects, but kept him awake and altered his temperament for the worse. His life revolved round the cycle of five days on-treatment, followed by a 3-week interval, then repeat. After his third cycle, he contemplated giving up because he felt so physically drained.

Two things kept him going. The first and most important was the immense support he received during his chemotherapy cycles, especially from his family, his future wife Stephanie and his 1975 classmates from Raffles Institution (including Professor John Eu-Li Wong and Drs Ngoi Sing Shang and Billy Tan). The second source of strength was remembering how he had persevered through the intense cold during marathons in the North Pole and Antarctica.

#### Into the light

Slowly, the wheelchair athlete found little ways to adapt (eg exercising with dumbbells, drinking Ensure and Prosure

since he had no appetite for solid food on treatment days) that made him feel less unwell after treatment. Between treatment cycles four and five, he even managed to complete an 84km ultramarathon to raise money for NUS Medicine. Dr Tan feels a close affinity to his oncologists, Dr Koh Liang Piu (at the National University Cancer Institute, Singapore) and Dr Benjamin Mow (in private practice), who went out of their way to help him with his treatment.

One year after his transplant, Dr Tan was back in his beloved racing wheelchair, competing in Berlin, Seoul, and Japan. First polio and now cancer could not stop him from doing what he loved. That bone marrow transplant in 2009 helped to free him from the onerous chemotherapy regimen. "I felt that it [the transplant] was my second lease on life and, with that, I should live my life and do more."

Doing more also included returning to medical practice in 2011 at NCCS. Again, he had to overcome obstacles such as convincing the Singapore Medical Council that he was in sufficiently good health to practice as a doctor. His first job as a doctor in Singapore involved looking after cancer patients who were undergoing chemotherapy, which he found very rewarding. However, in June 2016, he left for private practice to help support his brother and sister, who had both been diagnosed with cancer.

Dr Tan believes that, besides treating the body, encouraging the right mindset in patients is very beneficial. As someone who has never let illness or circumstances stop him from fulfilling his dreams, Dr Tan is himself a living example of the power of hope and a strong will. "Always embrace hope. Tomorrow will be a better day," he says.



Lotus Life Foundation, a Singapore-based charity focused on alleviating poverty both locally and in Nepal, is supporting the next generation of doctors and entrepreneurs through gifts totalling over \$\$1.2 million to the National University of Singapore (NUS) Yong Loo Lin School of Medicine and NUS Enterprise.

As part of this endeavour, the Foundation has established the Lotus-NUS Medical Bursary at NUS Medicine to offer medical students in financial need the chance to fulfil their potential. Up to four bursaries valued at \$\$33,600 each will be awarded each year for five years, starting from Academic Year 2017/2018. This is part of the Foundation's effort to promote the well-being of the future generations through providing better education and access to financial assistance for the focused, hardworking and talented individuals who deserve it most. The ultimate goal is for the students to achieve self-reliance and to make positive, productive contributors to society.

"Education is the cornerstone of any society. Education has profound economic, social and personal impact on individuals, families, communities and the nation. Good education instils in individuals a sense of responsibility towards society, humility towards fellow members of the community and enables them to make positive contribution to the development of the nation. We hope that the individuals benefitting from our gift will continue to work for the betterment of society and furtherance of our vision of promoting the well-being of our future generations," expressed Mr Nirmal Singh, Chairman of the Lotus Life Foundation.

Lotus Life Foundation has also pledged to NUS Enterprise

in support of establishment of Lotus-NUS Fund. Lotus-NUS Fund will provide seed funding for start-ups that are founded by Singaporean entrepreneurs and are involved in social enterprise projects. From 2017 to 2021, up to five entrepreneurs or companies will be awarded S\$25,000 each in funding each year to help them grow beyond ideation and to a stage where they can attract traditional venture capital funding.

The Foundation hopes that its gift will have a long-term impact and sees itself as a long-term partner for future social enterprises. "We hope the recipients of seed funding will be able to convert their ideas to workable social enterprises that will have explicit social and environmental impact. The Lotus Life Foundation provides a range of support to help social enterprises from startup to mature stages, such as access to external funding, training and advisory services, as well as access to relevant networks," said Mr Singh.

NUS President Professor Tan Chorh Chuan said, "We are honoured that the Lotus Life Foundation has chosen NUS as a recipient of their philanthropic support. Their generosity will enable the University to provide opportunities for outstanding young people to excel and to nurture entrepreneurial leaders with a strong sense of social responsibility. We hope this gift will inspire others to similarly support the University in developing our students' potential and fostering new ideas that will make a positive impact on society."

This story was first published on April 6, 2017 on NUS Giving at https://nus.edu/2sYJAiP.



Philanthropic support for MERCI, part of the NUS Yong Loo Lin School of Medicine, fosters innovations that have the potential to benefit millions of patients.

An electronic device that rotates bedridden patients' bodies to prevent them from developing bed sores. A removable barrier in the stomach that helps resolve Type 2 diabetes by limiting the absorption of food and creating a feeling of fullness.

These are just two innovations to improve the lives of patients that were taken from concept to reality thanks to gifts to the Medical Engineering Research & Commercialization Initiative (MERCI) at the Department of Surgery at the NUS Yong Loo Lin School of Medicine.

"It is very challenging to obtain funding to transform an idea from being just an idea into a tried and tested proof of concept that can be used to apply for government or other grants. These philanthropic gifts provide a much-needed leg up for our team who are working hard to understand what clinicians need and to translate those needs into products that will make a difference to patients' lives," shares Professor Lee Chuen Neng, Chair, MERCI.

Mr Prajogo Pangestu supported MERCI as a seed gift partner in 2009 to support groundbreaking research in medical devices. His gift has contributed to MERCI's success by enabling the team to address many of today's top medical conditions by bringing innovations to patients to help reduce suffering and improve the quality of patient care.

MERCI has many innovations under its belt. The Flipod, the product of a collaboration with the NUS Division of Industrial Design, provides unsupervised body rotational movement for bedridden patients. It is designed to reduce sleep disruption, and has the benefits of being small, portable and affordable.

The Gastroduodenal Sleeve (GDS), designed to resolve both Type 2 diabetes and obesity, mimics the effects of bariatric surgery, where parts of the stomach and intestines are removed to reduce weight and bring diabetes into remission. The GDS is a safe, minimally invasive and reversible solution that is endoscopically inserted and anchored in the stomach. By occupying space in the stomach, the GDS prevents the absorption of food and reduces appetite. It can easily be removed at the end of the treatment.

"The gifts to MERCI have a multiplier effect: they have the potential to change the lives for the better of not one patient but millions of patients. Moreover, they are part of the creation of an ecosystem, providing rewarding career opportunities for many, where medical technology solutions are conceptualised and eventually produced. These devices provide practical solutions to benefit patients in Singapore, across the region, and throughout the world," explains Prof Lee.

This story was first published on February 14, 2017 on NUS Giving at https://nus.edu/2sJCZo2.

#### PEOPLE OF NUS MEDICINE



## IT'S A MATTER OF BREEDING

There are 21 occupants in Jessie Tan's four-room HDB apartment. There's her sister, her parents and Jessie. And there're also 17 hamsters.

So many fur balls, you say. That's actually down from the 175 hamsters that populated Jessie's home a few years ago and which made life in her apartment rather interesting, before the numbers dwindled through natural attrition. Life is less frenetic though it is still packed these days for the life sciences graduate, whose day job is in research space administration.

After hours, it's quality time with her eighth generation of hamster breeds and hybrids — the Campbells (not the soup), Djungarians, Romulans, Klingons (just kidding) — as well as her boyfriend, who has to endure the competition for Jessie's attention.

Spend long enough time with someone, she says, and you get to know that person rather well. And so it is with her (we're talking about hamsters here) pets. So, after nearly two decades of hamster breeding that involved more than 200 of

the tiny creatures, Jessie is a veritable expert on the rodents.

Each of her pets is an individual, identifiable through its character, appearance, colour, habits and responses to training. For instance, the animals can be trained to react in a particular way through the use of sounds and sights. They also "interact" (Jessie-speak for hamster-squeak) with one another, squabble like human siblings and develop different behaviours during maturity. In fact, Jessie says hamster couples even experience mid-life crises, much like us homo sapiens. To the extent that one half of a hamster couple could turn its back on its partner. Really.

"I believe that your nature is one thing, and your upbringing is another," says Jessie. In other words, it comes down to pedigree. And so it is too with hamsters, which breed exponentially like, um, rabbits, thus accounting for that 175-strong colony a few years ago. But in case you think Jessie's only about little furry creatures, she wants you to know she's also an avid traveller and explorer of local food.

Still, there's no mistaking her fondness for the animals, which are classified as rodents belonging to the subfamily Cricetinae. And she's ready and willing to ham it up with anyone keen and curious enough to want to know more about these short-sighted and colour-blind omnivores. All that's needed to get a lively discussion going with Jessie? In your best Potter voice, exclaim, "Mesocricetus auratus!"

#### **INSIGHTS**



#### A SPECIAL FRATERNITY

By Dr Alvin Tan Kian Wei (MBBS Class of 2017) looks back on his undergraduate days.

"Not pride of knowledge, but humility of wisdom" This is the motto that no medical student will be unfamiliar with. These were the words that were ingrained in all medical students at the beginning of the university year when we first matriculated. It serves to remind us medical students that as we progress along our medical studies and gain new knowledge, we should always remain humble. Humility is not eating humble pie; it is a personal outlook that recognises our finiteness, and our need to continually learn from everyone around us – professors, mentors, friends and most importantly, our patients.

And now, five years on, its significance can't be any greater than before we graduate and start practicing as doctors. It has been a long five years of medical education, an experience that will remain with all of us for a lifetime.

What makes the NUS medical fraternity so special is that it is a tight knitted community that morphs from schoolmates to colleagues in the hospitals. People may think that medical school is all work and study, but the reality is, the medical fraternity consists of students who are not only into academics, but also very much engaged in sports, the arts and culture and service to the community.

There were many opportunities for medical students to showcase their talents out of medical school, such as the Annual NUS Rag and Flag event where students put up an arts performance to raise funds for a charity organisation; the annual Inter-Faculty Games, where faculties compete against each other in different sports such as swimming, tennis, squash, chess etc. and the annual Medicine Playhouse event where each batch comes together to write an original script and put up an hour's long play. These events bring us closer together, to understand how each individual in Medicine is special in his and her own way, and helps us learn to tap on each other's' strengths and help make up for each others' weaknesses.

More importantly, there were many others who have spent countless number of hours to teach us, friends who have walked us through the long arduous journey and all the patients we encountered in the hospitals who themselves have been mentors in teaching us invaluable lessons. A big thank you to those who have helped us and impacted us along the way. I look back on the five years at the NUS Yong Loo Lin School of Medicine and have no regrets that this is the university life I sought, and found.



## WHAT THE LIVING CAN LEARN FROM THE DYING

By Dr Noreen Chan Head & Senior Consultant, Division of Palliative Care, National University Cancer Institute, Singapore (NCIS)

A previous article mentioned the widespread (mis) perception that Palliative care is depressing and disheartening. What is less often discussed is how and why Palliative care workers keep doing what they do, and seem rather contented doing it. The hours are long; we deal with pain, loss and other difficult issues; it's hardly a glamorous career... in fact a wag once described my work as "a dead end job" (ha ha).

I personally get back so much more than I give. Caring for patients and families, and working with the medical

teams who look after them, has taught me so much that cannot be found in textbooks. About the science and art of medicine, the miracle and mystery of human existence and relationships, and most of all about myself. Let me share a few examples:

#### It may never be the "right time", but now is all we have

47-year-old Mr K was trying his best to cope. With the cancer, the pain, the chemotherapy, the inability to work. Talk to your wife and kids we said. "It's not the right time". His disease grew through conventional chemotherapy, so he was offered a trial treatment. Once again he was advised to talk to his family, to prepare for the worst. "It's not the right time" was his consistent answer. And on it went, until he was admitted to hospital in extremis, too breathless to speak, barely able to recognise his distraught relatives. It would never be the right time, but now there was no time left.

So don't wait to show your appreciation, say you're sorry and I love you, let your loved ones know what you want and don't want. If it's important, don't wait. There may never be a "right" time, but you never know, it might be the only time.

#### **INSIGHTS**



#### The things that matter most at the end of life aren't "things"

Surveys conducted across different countries have shown common themes about what people would value at the end of life. A minority prioritised life prolongation, the majority preferred comfort, being at peace, having loved ones present, and not burdening family members. Surveys that have been conducted in Singapore by the Lien Foundation show similar findings, with respondents indicating a range of concerns, including being a burden to others.

Some of my older patients tell me "my children are all grown up with their families, no need to worry anymore". Others are less assured, especially those with elderly parents or younger children, and they may feel guilty about not being able to continue with their responsibilities and roles. A few express regrets, usually about not spending more time with family, not valuing relationships more, not appreciating what they had.

#### People can grow

While it is true that many people die as they have lived, many can overcome the ingrained habits of a lifetime, to discover something new about themselves. These is a Chinese saying 活到老,学到老 which literally translates into "Live till you are old, learn till you are old". Serious illness and dying can be opportunities to learn and to grow, for patients and families.

People used to being in charge have had to learn to stop needing to "run the show", and accept that ceding control does not dent their dignity. Their partners, used to a more passive role, have had to step up, be more proactive. As physical health deteriorates, many have found ways to adapt to their changing circumstances, to strengthen themselves spiritually and emotionally, and to find peace.

#### Discovering the capacity for joy

A patient, G and I looked back over the year that we had shared together, in the knowledge that she might have only a few months ahead of her. She told me "It sounds strange, but there have been times I have felt so much joy, I can't explain it". That is not to say it had been a smooth ride – in fact there were many struggles and difficult times, including once when she nearly died — but I understood what she was talking about.

She was not referring to fireworks and "big bang" occasions, but everyday activities like family prayers at the dining table, listening to the children's stories of their day at school, quiet moments with her husband. As the great poet Tagore had written "The butterfly counts not months but moments, and has time enough." G, like the butterfly, mindfully and gratefully cherished every one of them.

#### INSIGHTS

#### It's not about how old you are

Wisdom is to be found everywhere, and is not the prerogative of adults. Kids really do say the darnedest things, and their honesty can be refreshing, funny and eye-opening. In my experience, even young children, especially when emotionally supported and secure, are able to come to their own sense of understanding and acceptance. What unsettles them is when the adults around them are upset and no one is explaining anything to them.

I once overheard the 8-year-old son of a patient solemnly tell his 6-year-old sister, that "God answers every prayer, but it may not be the answer we are looking for." Another, a 5-year-old, told by her father that mummy would be leaving them and going to heaven, replied, "Then she will be together with Ah Kong". Or 18 year-old J, who had always wanted to see the world but for his terminal cancer, deciding to donate his corneas so someone else would have the gift of sight.

#### **Finally**

So yes, there is a lot of suffering, fear, bewilderment, anger, loss and sadness... but there is also courage, joy, hope, resilience, creativity and love. Elisabeth Kübler-Ross wrote that "People are like stained-glass windows. They sparkle and shine when the Sun is out, but when the darkness sets in, their true beauty is revealed only if there is a light from within." And it has been my privilege to journey with patients and families, and to see that light shining through again and again.

#### Slowly and Steadily Like A Snail.

Rush

That's all we do

Rushing to go to the hospital to deliver that baby.

Rushing to learn how to walk and talk.

Rushing to school and avoid being late.

Rushing to be an all-rounder, getting all the accolade

Rushing to promote to higher education.

Rushing to get a job.

Rushing to get promotion after promotion.

Rushing to start a family.

Rushing to attain the FCs.

Rushing to get old.

Rushing to be a senior citizen.

Rushing to kick the bucket?

Is it all about rushing? Take a moment to pause and think. So much more is left behind in the midst of rushing. We should have used the time for our kith and kin. We should have given ourselves a break. Life presents us with one chance to live. Only one. Only you can answer whether it has been used well. At the end of your life, do not regret regrets.

Learn from a snail: slow and steady.



#### ETHICALLY SPEAKING



#### **A DUTY OF CARE**

By Associate Professor Jacqueline Chin, Centre for Biomedical Ethics (CBmE)

The discipline of bioethics can contribute actively to strengthening systems of care in our society, by engaging questions about what is owed to people growing old in Singapore and those who care for them. Supported by a gift from the Lien Foundation, a team from the Centre for Biomedical Ethics, The Hastings Center in New York and the Oxford Ethox Centre has researched and authored 10 new case studies on Caring for Older People in an Ageing Society. These will be added to an expanded 2nd volume of the free and open-access Bioethics Casebook (www. bioethiccasebook.sg), a teaching and learning resource for peer-to-peer education in healthcare ethics. The new collection reaches out to healthcare and social care professionals in the community working integrally with hospital doctors, nurses, and allied health professionals.

One of the case studies considers what is owed to caregivers of persons with impaired mental health. In Singapore, where mental illness — much like disability — is still considered a personal or family tragedy instead of an issue requiring

societal intervention, caregivers of psychiatric patients find themselves conscripted into a life of 'endless caregiving' with inadequate social support (Wong et al, 2015). In the case, elderly Mrs Kumar's hope of living just a day more than her son Rajeev reminds us how closely bound these two lives are, and how failing to ensure family-centred care for both patient and family caregivers can lead to both parties suffering harm. Mrs Kumar's failing health (she has just started dialysis) and exhaustion from the daily burden of caregiving threaten to incapacitate her completely. In that event, Rajeev's life and future are in danger of neglect. His well sibling, Amrita, also faces much uncertainty about what she would do for both her mother and brother.

Do health and social care professionals have obligations towards family members who are caregivers to their patients or clients? Social care professionals have fewer difficulties than healthcare professionals in recognising obligations to family members due to differences in the type of training they receive. This suggests that peer-to-peer education will be helpful in multi-disciplinary teams providing holistic care to patients and families.

Family-centred care addresses in practical terms the involvement of family members by explaining how they could support their loved one's participation in decisions, establish care routines, and keep a good balance between

#### ETHICALLY SPEAKING



a loved one's safety and well-being. This type of care includes assessing the caregivers' health and well-being, and making referrals for caregiver health needs and resources for family support. It would also attend to the capacity of individuals at home to provide ongoing care to the patient. For instance, a family-centred service would provide guidance to well siblings and other family members like Rajeev's sister Amrita, and his Aunt Madhu, about various ways to support Mrs Kumar and Rajeev.

Gitlin and Hodgeson (2016) note that healthcare professionals also face system barriers to family-centred care because health records are focused on information about patients and not much about caregivers. Healthcare reimbursements structures do not compensate doctors for taking additional time to assess a caregiver's health status and fitness to give care.

At the centre of this debate about caring for older people is the understanding of caring itself. The founding president of The Hastings Center, Daniel Callahan, declared that all people need care. We need care not only at the emotional level (respect, appreciation, humour, and the like), but also the cognitive level: we need those who care for our ways of thinking and how we frame our course of life. We need care at the level of our values, those who have an appreciation for the things that we cherish. Individuals also

see relationships with others in different ways, and being observant and sensitive to how someone interacts with different people is an aspect of caring.

As Callahan cautions, caring can be misplaced, and where a person might fall "within a spectrum of possible relationships" with a care recipient is important if the caregiver's work is to succeed in establishing a "healing, or helping, or consoling, or affectionate bond". As a society, what we owe to people growing old in Singapore and those who care for them, is care.

The 2nd Edition of the Singapore Bioethics Casebook was developed in consultation with over 180 health care and social care professionals from 40 organisations serving the health care and rehabilitation, home- and day-care, residential and social care needs of people growing old in Singapore, and was launched on May 24.

#### **REFERENCES**

- . Gitlin, L.N. and Hodgson, N.A. (2016). 'Who should address the needs of the care for a dementia patient's caregivers?' AMA Journal of Ethics, December, 18, 12: 1171-1181.
- Wong, R. and Ee, W. M. (2015), 'Social Impact of Policies for the Disabled in Singapore', In 50 Years of Social Issues in Singapore, 147-166

# SCHEDULER August – October

Date	Event & Venue
Aug 8	Flag Day
Aug 10	White Coat Ceremony University Cultural Centre, NUS
Aug 12	Rag Day University Town, NUS
Aug 18	Medical Grand Challenge Auditorium, NUHS Tower Block
Aug 24-26	Singapore International Infectious Disease Conference (SIIDC)  Grand Copthorne Waterfront Hotel, Singapore
Aug 25-27	6th Wong Hock Boon Paediatric Masterclass Auditorium, NUHS Tower Block
Sept 4-6	2nd Raffles Dialogue on Human Well-being and Security in 2030: The Critical Role of Innovation University Hall, NUS
Sept 9-10 Oct 7-8	Neighbourhood Health Service (NHS)  Eunos Crescent  Marine Terrace
Sept 19	Keynote Address 2017 Auditorium, NUHS Tower Block
Oct 6-8	13th Asian-Pacific Congress of Hypertension (APCH) Suntec City Convention and Exhibition Centre
Oct 12-13	Singapore Health and Biomedical Congress Singapore Expo
Oct 16	Awards & Appreciation Nite LT37, Level 3, Tahir Foundation Building (MD1)
Oct 21-22	Public Health Service (PHS) Jurong East

The NUS Medicine Total Workplace Safety and Health Implementation Committee launched the Best Poster Design Contest in the early part of this year. We are proud to announce the three winners:

#1 Loy Boon Pheng #2 Nur Sabrina Binte Yusri #3 VIVA-NUS CenTRAL







