MediCine

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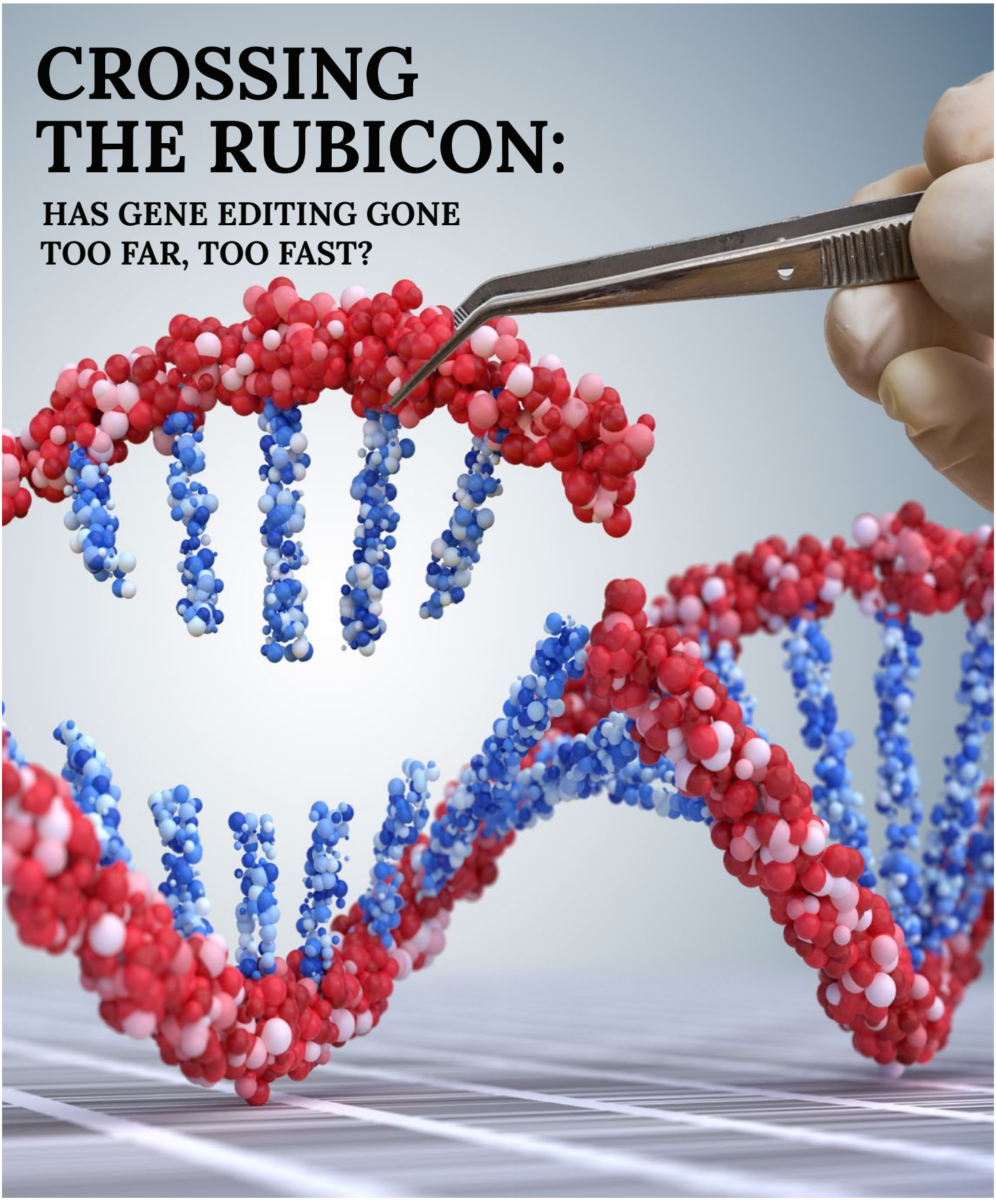

CROSSING THE RUBICON:

HAS GENE EDITING GONE TOO FAR, TOO FAST?

DEAN'S MESSAGE

Dear Reader,

Shortly, we will welcome about 560 young men and women of the Medicine and Nursing classes of 2024 and 2022 respectively. They will undergo a transformative educational experience over the next three to five years, one that will equip them with medical and nursing skills and knowledge to be effective healthcare providers. They will in time to come, join other NUS Medicine alumni in providing care for our community.

As the School cycles through a new academic year, our biomedical research work continues apace. This issue, we present a discussion on gene editing. It is a science that has come under a cloud caused by the controversial editing of the genomes of two babies born in China. In another marvellous piece of research work, our colleagues have found the reason for chronic rejection of transplanted organs. This opens the way for precision medicine in transplant, where specific immunosuppressive strategies can be devised to minimise transplant failure and reduce transplant patients' risk of getting infections and cancer. A third story that we are pleased to share with readers is about the speed at which the human brain processes and manages information: their finding gives new meaning to the phrase, quick thinking.

We have been turning out doctors for Singapore since 1905, and the work of our scientists has helped to influence and shape the practice of medicine here. That has and will always remain our mission. But the ways in which we work, teach and train and conduct biomedical science are changing, shaped by new technological advances in telemedicine, artificial intelligence, big data, to name just three of the revolutionary, disruptive global forces that are transforming the way we all live, work and play. The NUS medical school will harness the power of these advances to seek, exploit and harvest the new and exciting opportunities that will enable us to contribute even more meaningfully to health education and healthcare.

Wishing you an enjoyable read,

Yap Seng

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The Department in 1993: Assoc Prof Tsoi Wing Foo is seated, second from right.

ENSURING MENTAL HEALTH FOR ALL

The NUS Department of Psychological Medicine celebrates 40 years of education and research

In the past 40 years, much progress has been made in the field of psychiatry in Singapore. We have learnt more about the local mental health landscape and understood how our unique cultural and social issues impact the practice of psychiatry. At the heart of academic psychiatry lies the NUS Yong Loo Lin School of Medicine Department of Psychological Medicine. Started in 1979 with a small team of six people, we now have more than 30 academic, research and administrative staff working to push the boundaries of research and education in psychiatry.

The pioneering members of the Department were enthusiastic in research, and there was rapid development in this area. The founding Head of Department, Dr Tsoi Wing Foo, pioneered many studies in schizophrenia and transsexualism. Since then, research in the Department has branched out in numerous directions, ranging from looking into acute conditions to exploring how we can preserve the mental health of the well or at-risk populations. Our researchers have collaborated with numerous organisations to look into acute conditions such as depressive disorders, obsessive-compulsive disorder and schizophrenia to explore different aspects of these conditions, such as the neurobiological basis of mental illness.

Studying the ageing mind

In 1986, the NUS Department of Psychological Medicine was one of three centres selected for the World Health Organisation Global study of Dementia in Asia. The Department was also one of the three centres in NUS to be nominated as WHO research centres. The first study on dementia in Singapore was published in 1990, and this study was selected to be presented at the World Forum on Mental Health at United Nations in New York in 1999. The Department is currently the only department in Singapore that has been invited by the United Nations to speak in a World Forum.

Prof Kua Ee Heok delivering the Tan Geok Yin Professor of Psychiatry and Neuroscience Lecture in April 2018.

Through the years, research in the elderly population has grown in significance due to Singapore's ageing population. Thus, long-term cornerstone projects such as the Gerontology Research Programme and the Dementia Prevention Programme were established to conduct multi-disciplinary and collaborative research on a wide range of themes in gerontology, spanning the basic, clinical and behavioural sciences.

The Gerontology Research Programme, currently headed by Associate Professor Ng Tze Pin, has looked into various aspects of mild cognitive impairment and dementia. For instance, the Singapore Longitudinal Ageing Study (SLAS) has studied the epidemiology of various conditions in Singaporean elderly for the past 15 years. Various interventions have been examined to see if these conditions can be prevented or attenuated, and more than 180 scientific papers have been published.

Professor Kua Ee Heok, who has been with the Department since its very early days, has spent the past 38 years looking into various aspects of elderly psychiatry. "The research we have done for dementia prevention tells us that there is the possibility that we can prevent or delay the onset of dementia," he related, "and this would be tremendous, because the research is now translated to the community."

Choral singing is being evaluated by the Jurong Ageing Study to see if it can help the elderly at high risk of dementia to slow down or even prevent the onset of disease.

An Undefeated Mind: The Mind-Science Centre

More than a decade ago, the NUS Mind-Science Centre (MSC) was conceptualised by Professor Kua, Mr Wee Sin Tho, and Associate Professor Goh Lee Gan. It was to be a Centre of Excellence dedicated to research on factors that contribute to mental resilience, and to explore how social interventions contribute to the well-being of the various

Left to right: Assoc Prof John Wong, Prof Kua Ee Heok and Dr Alan Wallace, an international expert on mindfulness.

populations. The first project embarked upon was the Jurong Ageing Study (JAS), which looked at ageing in a cohort of elderly individuals in the western population of Singapore. The findings from JAS have been translated to the Age Well Everyday Programme, one of the key flagship programmes of the MSC.

Associate Professor John Wong, current Head of Department as well as the Head of the MSC, explained that the Centre is devoted to research in mental resilience across the age continuum. "The Mind-Science Centre looks at upstream prevention and programme development to serve the mental well-being of the well population as well as the at-risk population," he said.

For example, the Singapore Youth Resilience Scale (SYRESS) has been developed and validated as part of an effort to better characterise factors that contribute to tenacity in our school-going children. Research in our elderly population has continued, with various interventions such as choral singing, art therapy, horticultural therapy, and music reminiscence being studied to see how mental health can be improved. Indeed, much more research needs to be done so that we can build psychologically strong individuals, families and communities.

Teaching the next generation

In addition to research, the Department of Psychological Medicine also provides undergraduate training in psychiatry to fourth year medical students. Prior to 1972, the psychiatry teaching programme for medical students at the University of Singapore consisted of 20 hours of lectures, followed by a visit to the Woodbridge Hospital. Later, the clinical postings were increased progressively to two weeks, and subsequently four weeks. A longer clinical posting was needed to help the students develop a better understanding of mental health issues.

Today, our students undergo a six-week rotation through the Department, where they are immersed in the world of psychiatry and equipped with skills to engage with psychiatric disorders. Dr Cyrus Ho, the Deputy Undergraduate Director shared that while most medical graduates may not choose to specialise in psychiatry, it is still essential for them to recognise that mental and physical health are intrinsically linked. "As many of them

The Department of Psychological Medicine 38th Anniversary photo.

become generalists, or specialised in other disciplines, we make a deliberate effort to train them, and to expose them to a wide variety of medical conditions that interplay with psychiatry," he said.

The Department has received the Clinical Training Excellence Award for four consecutive years – it is a testament to the efforts of our educators and their commitment to educating the next generation of doctors and equipping them with the necessary knowledge and skills to identify, treat and support our patients with mental health conditions.

The Department is also highly involved in postgraduate training, for both our residents and specialists. The Psychiatry residency training programme is a dynamic enterprise comprising a clinical curriculum that allows the residents to rotate through multiple care settings. In addition, the Department has also been hosting the NUS Master of Medicine (Psychiatry) programme since 1985, allowing specialists to further develop their skills and knowledge base in important areas of psychological medicine.

The Department has also hosted conferences to share its work and stimulate further discussion of pertinent topics in psychiatry. In 2014, the inaugural NUS Academic Psychiatry Conference was launched, with international collaborators such as the Harvard Medical School and the University of Cambridge.

Later this year, the fifth Conference in the series will be held to look at Resilience Across the Age Continuum. This Conference brings together a dynamic panel of international speakers who will be able to deliver insights into the challenges and prospects of building resilience from the young to the old.

A partnership for our patients and community

The support of our counterparts working at the National University Hospital have also been essential in our continuous progress. Ward 33, the inpatient psychiatric ward, and the Neuroscience Clinic are staffed by the Department's psychiatrists, residents, psychologists and other allied health professionals. The Department also hosts many different programmes looking into various aspect of community mental health, such as the Women's Emotional Health Service and REACH (West), to name a few. Many of the doctors have offered their time and expertise in helping to teach and supervise our medical students. Our psychiatrists and psychologists have often also given valuable input by relating real life issues that impact translational research, as they best understand the intricacies of dealing with mental health conditions.

In the years to come, the NUS Department of Psychological Medicine will strive to excel in research and education. Interest in mental health conditions has increased over the years, leading to more willingness to learn and less readiness to stigmatise those struggling with mental health issues. Our efforts to broaden the field of psychiatry and to educate our next generation of doctors will sow the seeds for better mental health outcomes for all. Here's to another fruitful 40 years!

Group photo of speakers and discussants at the Resilience Roundtable.

RESILIENCE KEY TO MENTAL FORTITUDE

NUS Psymed Conference focuses on impact of adverse events on mental health, ability to cope with stress

The NUS Department of Psychological Medicine started the year with the 5th NUS Academic Psychiatry Conference. It was centred around the theme "Resilience Across the Age Continuum", a very pertinent theme in our day and age. With psychiatric conditions such as depression, anxiety and cognitive impairment on the rise, the spotlight focuses on whether such conditions can be prevented or staved off. Resilience reflects the fortitude of the mind in facing adversity, and thus forms an important component of our strategy to promote mental health in the general population. The conference thus sought to understand the various factors in resilience from the young to the old, and how we can build resilience in these subgroups. International experts from 16 different countries shared their views in these areas with delegates from various mental health professions, including medicine, psychology, nursing, school counselling and occupational therapy.

Four pre-Conference workshops featured domain experts in psychiatry - Dr Alan Wallace, President of the Santa Barbara Institute for Consciousness Studies, chaired the Mindfulness Workshop over four afternoons. The Neurocognitive Rehabilitation Workshop was led by Dr Isabelle Amado, the Director of the Reference Centre for Cognitive Remediation and Rehabilitation (C3RP) in Sainte Anne Hospital in Paris, France. Professor Robert Ursano, Director of the Center for the Study of Traumatic Stress and Chairman of the Department of Psychiatry at the Uniformed Services University of the Health Sciences in Maryland, USA, chaired the third workshop on Brief Psychodynamic Psychotherapy. The fourth - the Leadership Workshop - featured experienced psychiatrists such as Professor Kua Ee Heok, Professor Norman Sartorius, Dr Chee Kuan Tsee, Professor Chong Mian-Yoon and Associate Professor Tan Chay Hoon, who shared their insights and thoughts about leadership in medicine and psychiatry. The

Left to right: Dr Chris Tsoi, Dr Celine Wong, Prof Norman Sartorius, Dr Tian Cheong Sing, and Prof Kua Ee Heok, during the Public Symposium Q&A Session.

workshops sought to address apposite topics and areas of interest, equip clinicians with skills to better care for their patients, and further develop psychology and psychiatry in the context of the Singaporean population.

The Resilience Roundtable, held before the Conference, discussed several specific aspects of resilience, such as resilience in childhood adversity and trauma, as well as the role of technology and spirituality in resilience. There was also a lively discussion over the nature of resilience, where its biological, genetic and environmental factors were discussed. Various stakeholders in the community were invited to contribute their expertise and perspectives on these issues.

Over the weekend, the Mind-Science Centre held two talks at the Ngee Ann Kongsi Auditorium at the National Gallery Singapore. Dr Alan Wallace was invited to give a talk on Mindfulness to the volunteers of the Age Well Everyday programme spearheaded by the Mind-Science Centre. In the afternoon, a public symposium was organised on the theme "Mental Health in the City: Living, Working and Ageing in Singapore". Professor Norman Sartorius, Inaugural Speaker of the Tow Tiang Seng Distinguished Lecture Series, delivered the 5th Lee Kim Tah Lecture. Three clinicians, Dr Celine Wong, Dr Tian Cheong Sing and Dr Chris Tsoi delivered other talks on various aspects of mental health relevant to Singaporeans.

The Conference proper, held over a two-day period, was launched by Professor Chong Yap Seng, Dean of the NUS Yong Loo Lin School of Medicine. Professor Norman Sartorius delivered the keynote lecture on the topic of global mental health, and the first symposium followed, looking into ageing and preventative health. Researchers in this field shared about the interventions that they developed and trialled in large cohorts with the aim of promoting and sustaining mental resilience in the elderly. Intergenerational interactions, cognitive training, aerobic exercise, and choral singing were discussed as means by which communities of elderly people could come together to strengthen their minds.

The second symposium was on public health and epidemiology. Professor Ursano delivered the plenary lecture on resilience in adversity, looking how we can build the core of resilience even in trying and traumatic circumstances. Other speakers shared about their work in public health efforts to build resilience, including understanding the effects of natural disasters on the human psyche, looking at how loneliness and ageing affects resilience, and how positive mental health and well-being can be built.

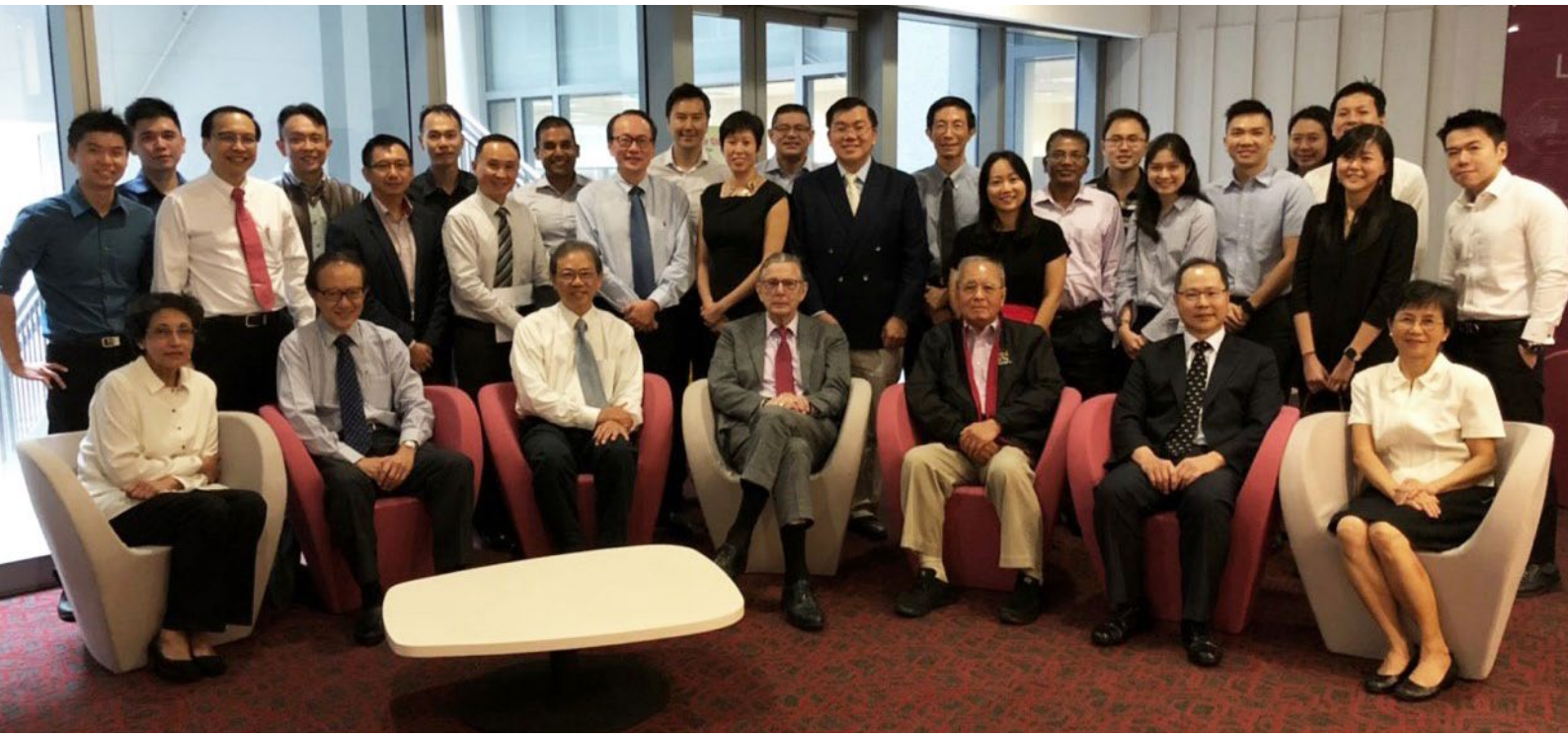
Day 2 opened with a plenary lecture by Dr Becky Inkster on the effects of digital innovation on mental health services. A diverse range of speakers shared about other aspects of digital mental health, with topics such as using digital tools to optimise healthcare, and developing smartphone apps to prevent suicide and to cope with stress or mild depression.

A summary of the Resilience Roundtable was also presented at the Conference by Professor Ursano and Professor Frank Verhulst. Though it was but a short two days, there was much discussion and sharing, and the delegates who attended the Conference had a fruitful time.

Ms Sim Ann, Guest of Honour at the Greater Good Series Dinner, with Mrs Teo Poh Yim, Patron of the Mind-Science Centre.

To end the Conference, as well as to mark the 40th Anniversary of the Department of Psychological Medicine, the Greater Good Series Dinner was held with over 200 guests, many of whom are former department staff. Ms Sim Ann, Senior Minister of State, Ministry of Communications and Information and Ministry of Culture, Community and Youth, delivered the opening address on community resilience.

The 5th NUS Academic Psychiatry Conference saw one week with a flurry of activity, but has left behind much to think about and act upon. At the dinner, Professor Sartorius parted with these words: "Resilience is a big goal, and it requires attention and involvement from all of us." Indeed, all of us must think about what resilience means to us, and how we can develop it in ourselves, in those around us, and together as a community.



Speakers, discussants and participants of the Leadership Workshop.

EAST WEST DIALOGUE AT NUHS-HARVARD BIDMC CONFERENCE

By Dr Adrian Kee
Senior Consultant, Division of Respiratory and Critical Care Medicine, University Medicine Cluster, National University Hospital
Programme Director, NUHS Internal Medicine Residency Programme

The fourth edition of the NUHS-Harvard BIDMC Conference – Updates in Internal Medicine was held on 25-27 January 2019. Beth Israel Deaconess Medical Centre (BIDMC) is a major teaching affiliate of the Harvard Medical School (HMS) and has collaborated closely with the NUHS in areas of education and research. Building on the successes of the previous three conferences, this year's overarching theme – "When East Meets West" – was aptly brought about by the first of two keynote talks.

NUHS Chief Executive Professor John Eu-Li Wong kicked off the conference by speaking on "The Evolving Health Care Model from an Asian Perspective." It was followed by "The Evolving Health Care Model from an American Perspective", delivered by Professor Mark Zeidel, Chief of Department of Medicine in BIDMC.

After both keynote addresses, conference participants turned their attention to the programme's five contemporaneous focus areas: Oncology, Ageing, Metabolic Diseases, Infectious Diseases and Gastroenterology & Hepatology. They were treated to informative sessions tailored to bring them up to speed with current, relevant and important developments in these focus areas. Eminent faculty from BIDMC served as conference speakers – Professors Mark Zeidel, Sanjiv Chopra, Lowell Schnipper, Martin Abrahamson and Christopher Smith.

Participants of the Medical Jeopardy game segment from NUHS, SHS and NHG, together with their programme directors.

Professor Adeeba Kamarulzaman (Dean, Faculty of Medicine, University of Malaya), Professor Sanjiv Mahadeva (Head of Academic & Clinical Services, Department of Medicine, UM) and inspiring local faculty from NUHS and Tan Tock Seng Hospital also lent weight to the line-up of speakers. The talks were specially prepared such that the content was immediately relevant and beneficial to Internal Medicine residents who were looking for quick updates of the knowledge applicable to their day-to-day practice.

A special feature this year was the inclusion of parallel sessions related to medical education. Associate Professor Christopher Smith, Associate Chair of Education in the Department of Medicine in BIDMC, conducted several sessions ranging from effective clinical teaching, assessment of learning to cognitive learning theories. These sessions were attended by residents and faculty members and saw fruitful engagement and exchanges of good ideas.

The conference came to a rousing close on a bright Sunday morning where Internal Medicine residents from NUHS, Singhealth (SHS) and National Healthcare Group (NHG) pitted their knowledge and wits against one another in the Medical Jeopardy gameshow segment. Modelled after the all-time favourite gameshow "Jeopardy", this version featured challenging medical questions designed to test the depth and breadth of the residents' medical knowledge. It was a thoroughly enjoyable game, culminating in a nail-biting finish where NUHS and NHG battled for top honours. It came down to a tie-break question, with the NUHS team prevailing to lift the Challenge Trophy on home soil. Our heartiest congratulations to the team comprising Drs Lim Wei Yang, Joshua Tan and Nicole Chong.

Over the course of 2.5 days, more than 100 participants benefited from the knowledge sharing in the focus areas and were brought up to speed with the advances and current expert management strategies. The conference not only provided a learning platform for participants, but also gave opportunities to network with local and international experts and peers. We hope that the conference rejuvenated and inspired participants to give of their best during their training and in their daily clinical practice.

MUSHROOMS MAY REDUCE RISK OF COGNITIVE DECLINE

A team from the Department of Psychological Medicine and Department of Biochemistry at the NUS Yong Loo Lin School of Medicine has found that seniors who consume more than two standard portions of mushrooms weekly may have 50 per cent reduced odds of having mild cognitive impairment (MCI).

A portion was defined as three quarters of a cup of cooked mushrooms with an average weight of around 150 grams. Two portions would be equivalent to approximately half a plate. While the portion sizes act as a guideline, it was shown that even one small portion of mushrooms a week may still be beneficial to reduce chances of MCI.

"This correlation is surprising and encouraging. It seems that a commonly available single ingredient could have a dramatic effect on cognitive decline," said Dr Feng Lei, who is from NUS Psychological Medicine, and the lead author of this work.

The six-year study, which was conducted from 2011 to 2017, collected data from more than 600 Chinese seniors over the age of 60 living in Singapore. The study was carried out with support from the Life Sciences Institute and the Mind Science Centre at NUS, as well as the Singapore Ministry of Health's National Medical Research Council. The results were published online in the Journal of Alzheimer's Disease on 12 March 2019.

MCI is typically viewed as the stage between the cognitive decline of normal ageing and the more serious decline of dementia. Seniors afflicted with MCI often display some form of memory loss or forgetfulness and may also show a deficit in other cognitive functions such as language, attention, and visuospatial abilities. However, the changes can be subtle, as they do not experience the disabling cognitive deficits that affect everyday life activities, which is characteristic of Alzheimer's and other forms of dementia.

"People with MCI are still able to carry out their normal daily activities. So, what we had to determine in this study is whether these seniors had poorer performances on standard neuropsychologist tests than other people of the same age and education background," explained Dr Feng. "Neuropsychological tests are specifically designed tasks that can measure the various aspects of a person's cognitive abilities. Some of the tests we used in this study were adopted from a commonly used IQ test known as the Wechsler Adult Intelligence Scale."

The researchers conducted extensive interviews and tests with the senior citizens to determine an accurate diagnosis. "The interview takes into account demographic information, medical history, psychological factors, and dietary habits.

Mom was right: eat your mushrooms. Dr Feng Lei (left) and Dr Irwin Cheah (right).

A nurse will measure blood pressure, weight, height, handgrip, and walking speed. They will also do a simple screen test on cognition, depression, anxiety," said Dr Feng. After this, a two-hour standard neuropsychological assessment was performed, along with a dementia rating. The overall results of these tests were discussed in depth with expert psychiatrists involved in the study to get a diagnostic consensus.

Six commonly consumed mushrooms in Singapore were referenced in the study. They were golden, oyster, shiitake, white button mushrooms, as well as dried and canned mushrooms. However, it is likely that other mushrooms not referenced would have also indicated beneficial effects. The researchers believe the reason for the reduced prevalence of MCI in mushroom eaters may be down to a specific compound found in almost all varieties. "We are very interested in a compound called ergothioneine (ET)," said Dr Irwin Cheah, Senior Research Fellow from NUS Biochemistry. "ET is a unique antioxidant and anti-inflammatory which humans are unable to synthesise on their own. But it can be obtained from dietary sources, one of the main ones being mushrooms."

An earlier study by the team on elderly Singaporeans revealed that plasma levels of ET in participants with MCI were significantly lower than age-matched healthy individuals. The work, which was published in the journal Biochemical and Biophysical Research Communications in 2016, led to the belief that a deficiency in ET may be a risk factor for neurodegeneration, and increasing ET intake through mushroom consumption might possibly promote cognitive health.

Other compounds contained within mushrooms may also be advantageous for decreasing the risk of cognitive decline. Certain hericenones, erinacines, scabronines and dictyophorines may promote the synthesis of nerve growth factors. Bioactive compounds in mushrooms may also protect the brain from neurodegeneration by inhibiting production of beta amyloid and phosphorylated tau, and acetylcholinesterase.

The potential next stage of research for the team is to perform a randomised controlled trial with the pure compound of ET and other plant-based ingredients, such as L-theanine and catechins from tea leaves, to determine the efficacy of such phytonutrients in delaying cognitive decline. Such interventional studies will lead to more robust conclusions on the causal relationship. In addition, Dr Feng and his team also hope to identify other dietary factors that could be associated with healthy brain ageing and reduced risk of age-related conditions in the future.

NO MERE GUT FEELING

Blastocystis unmasked as a killer of good bacteria

Dr Chin Wen Png, postdoctoral research associate at the Department of Mircobiology and Immunology, at work.

Since most of the microbes in our gut are bacteria, they tend to hog much of the microbiome research limelight. But, lurking amongst the bacteria are other microbes such as single-cell eukaryotes (SCE) and viruses, which have been largely ignored until now. If doctors and scientists think of Blastocystis (one of the most common gut SCEs) at all, they often regard it as a harmless commensal organism, peacefully co-existing with its bacterial neighbours. However, that could change with the publication of a new study from NUS Medicine (online in Microbiome on 11 March 2019), which shows that a subtype of Blastocystis isolated from the stools of a hospital patient with gastrointestinal problems in Singapore can actually harm its neighbours and its home in an insidious way.

In fact, Associate Professor Kevin Tan and Associate Professor Zhang Yongliang from the Department of Microbiology and Immunology at NUS Yong Loo Lin School of Medicine (NUS Medicine), together with postdoctoral research associates John Yason and Chin Wen Png, demonstrated that Blastocystis subtype 7 (ST7) selectively caused the death of Bifidobacterium (one of the "good" bacteria in the body) in cell culture and in vivo.

The ST7 strain of Blastocystis appeared to induce oxidative stress mechanisms, which involve the release of reactive oxygen species (ROS). These killer molecules caused the death of the good Bifidobacteria. Interestingly, the Blastocystis ST7 organisms also reduced the population of Lactobacillus (another good bacteria) in vivo, although the mechanism of killing is still unknown.

Bifidobacterium and Lactobacillus are considered good bacteria because they maintain the integrity of the intestinal lining by supporting tight junctions, which act like cement between the cells that make up the lining. They are also commonly used as probiotics to promote gut health. Besides killing Bifidobacterium directly, Blastocystis ST7 can also gang up with E. coli in the gut to kill even more of these protectors. The researchers also found that ironically, Bifidobacterium and E. coli both help Blastocystis grow better. In other words, Bifidobacterium promotes the growth of its own killer.

To make matters worse, Blastocystis ST7 injures the gut lining directly as well as indirectly by triggering an inflammatory response, causing lesions (ulcers) and a disordered structure of the intestinal lining in vivo.

Assoc Prof Kevin Tan (left) and Assoc Prof Zhang Yongliang from the Department of Microbiology and Immunology.

Add to this the loss of the protective good bacteria, an infection with Blastocystis ST7 could be a recipe for long-term damage to the gut lining, possibly contributing to inflammatory bowel disease, irritable bowel syndrome, as well as gastrointestinal and colon cancers.

Part of the reason for the unclear role of Blastocystis in disease is that previous studies did not consider the Blastocystis subtype that was being investigated. Some subtypes are likely to be harmless, but this study shows that ST7 is uniquely different. Not only does ST7 have harmful effects, it is also resistant to metronidazole, the typical treatment for Blastocystis. Like other Blastocystis subtypes, ST7 is transmitted through eating food that has been contaminated with faeces from infected animals, especially birds. Although ST7 has been reported mainly in Singapore, it has also been described in Japan and in at least one Danish study. Thus, this pathogenic Blastocystis subtype could be found in other ethnicities and geographic locations as it becomes more widely studied.

Assoc Prof Tan is already developing tools to study the mechanisms by which Blastocystis causes disease in greater depth. He and his team have established a genetic modification system for Blastocystis, whereby foreign genes can be introduced into and expressed in Blastocystis and the effects of these changes can be studied. They hope to use this system to illuminate how Blastocystis interacts with its host to cause disease and to explore ways to combat the microbe.

"This is the first detailed study to show a causal link between Blastocystis, a common single cell eukaryote of the human gut, and the host microbiota. We reveal how it reduces the numbers of beneficial bacteria, which may in turn lead to an unbalanced gut microbiome and poorer gut health," he said.

The detrimental effects of Blastocystis on Bifidobacterium and Lactobacillus could facilitate the development of inflammatory bowel disease and irritable bowel syndrome, in which the good bacteria play a protective role. Based on these results, doctors may want to consider excluding faecal transplants that contain specific subtypes of Blastocystis during faecal microbiota transplantation.

From left: Assoc Prof Paul MacAry, NUS Medicine Department of Microbiology and Immunology and Prof A. Vathsala, Co-director of NUH's NUCOT.

TRANSPLANT ORGAN REJECTION – RESEARCHERS GAIN NEW INSIGHTS

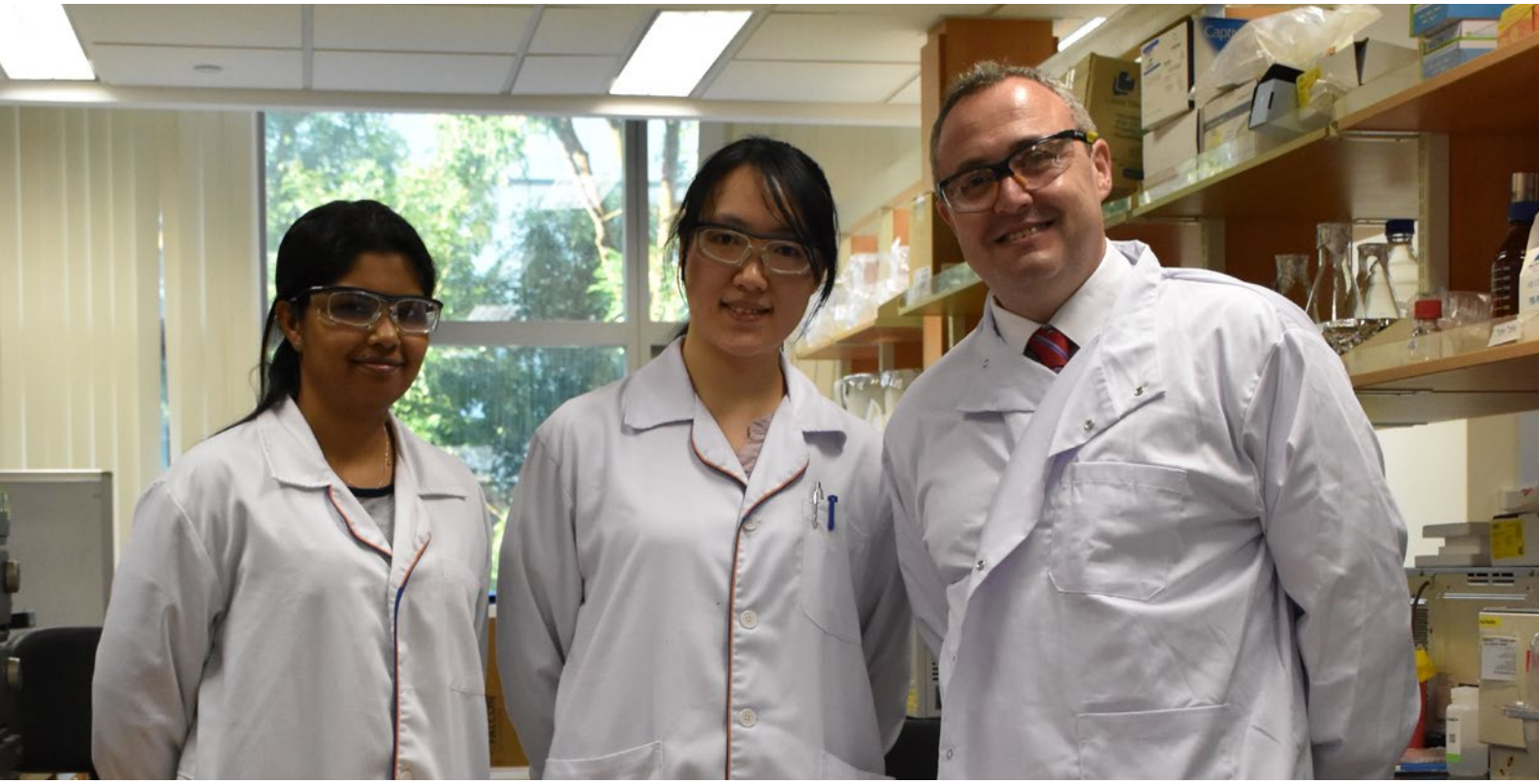
Rejection of any kind is always hard to deal with, but when one's body rejects a precious organ transplant, the consequences can be devastating. Professor A. Vathsala, Co-director of the National University Centre for Organ Transplantation at the National University Hospital (NUH) and Professor of Medicine, shared that between 30% to 40% of kidney transplants are lost over time to rejection. She, together with Associate Professor Paul MacAry of the Department of Microbiology and Immunology at NUS Medicine, decided to collaborate on addressing one major clinical problem at NUH's NUCOT: How to make each transplanted organ last longer?

Introducing an organ from a donor into a recipient almost always leads to the recipient's immune system recognising the new organ as foreign and mounting an immune response. Transplant (or graft) rejection can be categorised into two main types: cell-mediated rejection and antibody-mediated rejection. Cell-mediated rejection, which occurs more commonly within the first year after a transplant, is caused by immune cells called T cells attacking the transplant. This type of rejection responds well to treatment with non-specific immunosuppressants such as steroids.

The particularly thorny issue for transplant patients is antibody-mediated rejection, which causes chronic rejection. Antibodies in the transplant patient bind to a molecule called human leukocyte antigen (HLA) on the transplanted donor organ and stimulate an inflammatory response involving either immune cells or the complement pathway. One major problem in transplantation is the difficulty in diagnosing and predicting antibody-mediated rejection. Moreover, doctors only find out that rejection has occurred when a graft starts to fail and they perform a biopsy.

"We found that up to twenty percent of patients had antibodies against their donors. Just because a patient has antibodies doesn't mean they are going to have a rejection. Although many transplant patients have antibodies, not all antibodies are harmful and to date there is not a good way to predict which antibodies are actually harmful," said Prof Vathsala.

Another, bigger problem is that there are no effective treatments for antibody-mediated rejection. Such patients with antibody-mediated rejection end up needing re-transplantation with a fresh organ, which is challenging given the shortage of donor organs. Hence, antibody-mediated rejection is a major challenge in organ



Assoc Prof Paul MacAry with his team.

transplantation and presents an ideal target for pushing the envelope on transplant outcomes.

A critical step in antibody-mediated rejection is the binding of antibodies in a transplant recipient to the donor HLA molecule. These antibodies are called alloantibodies. However, until now, the mechanism by which these antibodies bind to HLA was not known. In a paper published online in Nature Communications on 21 February 2019, Assoc Prof MacAry, Prof Vathsala, along with collaborators from Nanyang Technological University and Oxford University, announced the first high-resolution crystal structure of the alloantibody-HLA interaction.

At this resolution (2.4 angstroms), the researchers were able to glean several important insights. Firstly, they identified two amino acids in HLA (aspartic acid at position 90 and arginine at position 14) that were critical for the antibody-HLA binding. Secondly, they found that the antibody bound to a site at the bottom of the HLA protein, some distance away from the sites at which peptides, T cells and natural killer cells bind to HLA. This finding was surprising because it indicated that the inflammatory response stimulated by the antibody was independent of the interactions of peptides or immune cells with HLA.

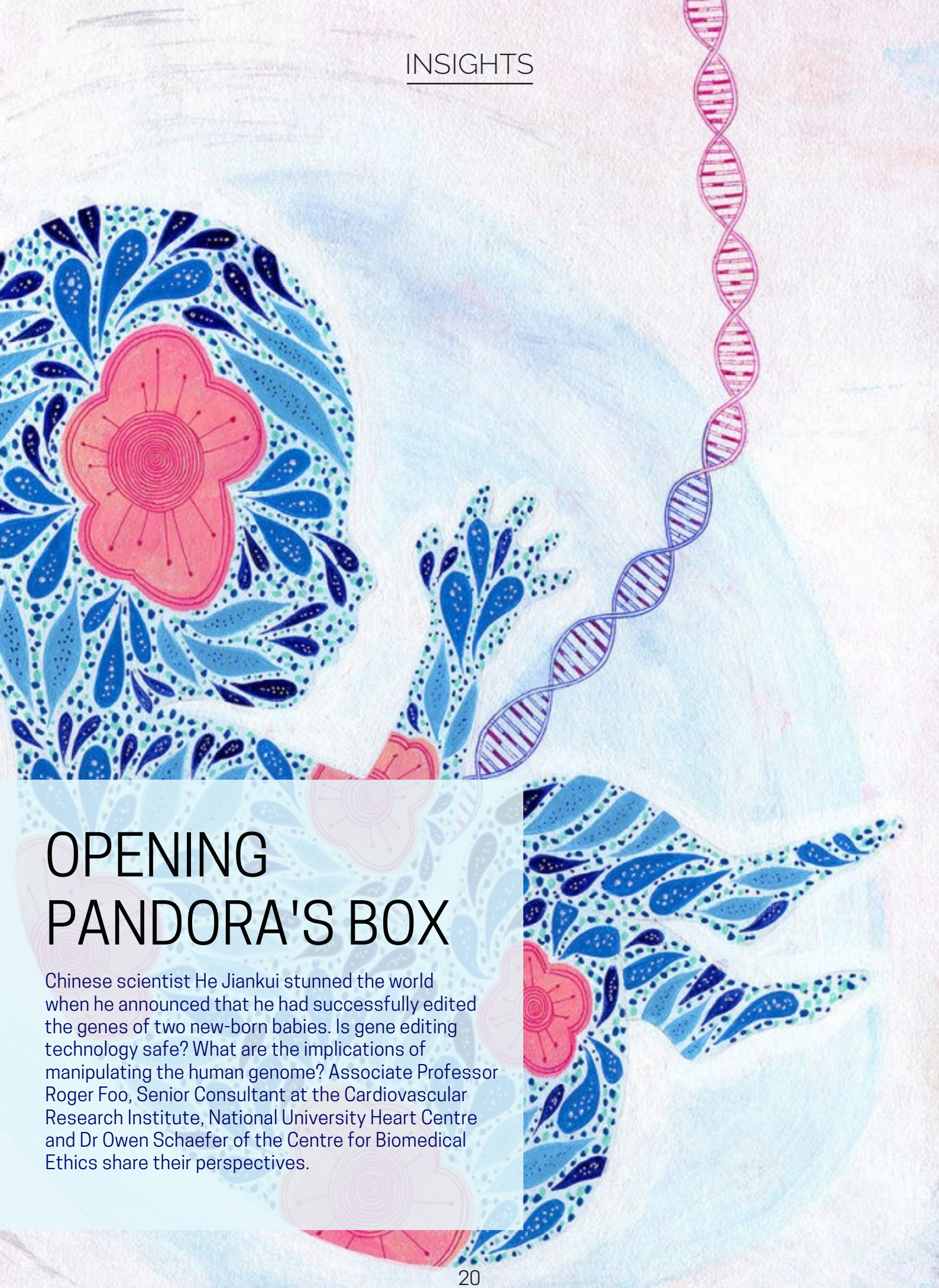
"What was interesting is that the antibody binds to the side of the [HLA] molecule," explained Assoc Prof MacAry. "What this allows you to do is design inhibitors that are going to obstruct the interface because if you stop the antibodies binding, you stop those antibodies from engendering the immune attack."

In fact, the team showed that one form of the antibody (a subclass called IgG4) bound to the HLA protein without causing an inflammatory response. Since these antibodies are able to reduce inflammation by binding to HLA and preventing other antibody subclasses from binding, they could be developed as therapies for prevention or treatment of antibody-mediated rejection.

According to Professor Kathryn Wood, Emeritus Professor of Immunology at the University of Oxford and the Khoo Oon Teik Professor of Surgery at NUS Medicine, who was an advisor for the project and a co-author on the Nature Communications paper, this is a "landmark study that all groups around the world will take note of. It's really a first in this field."

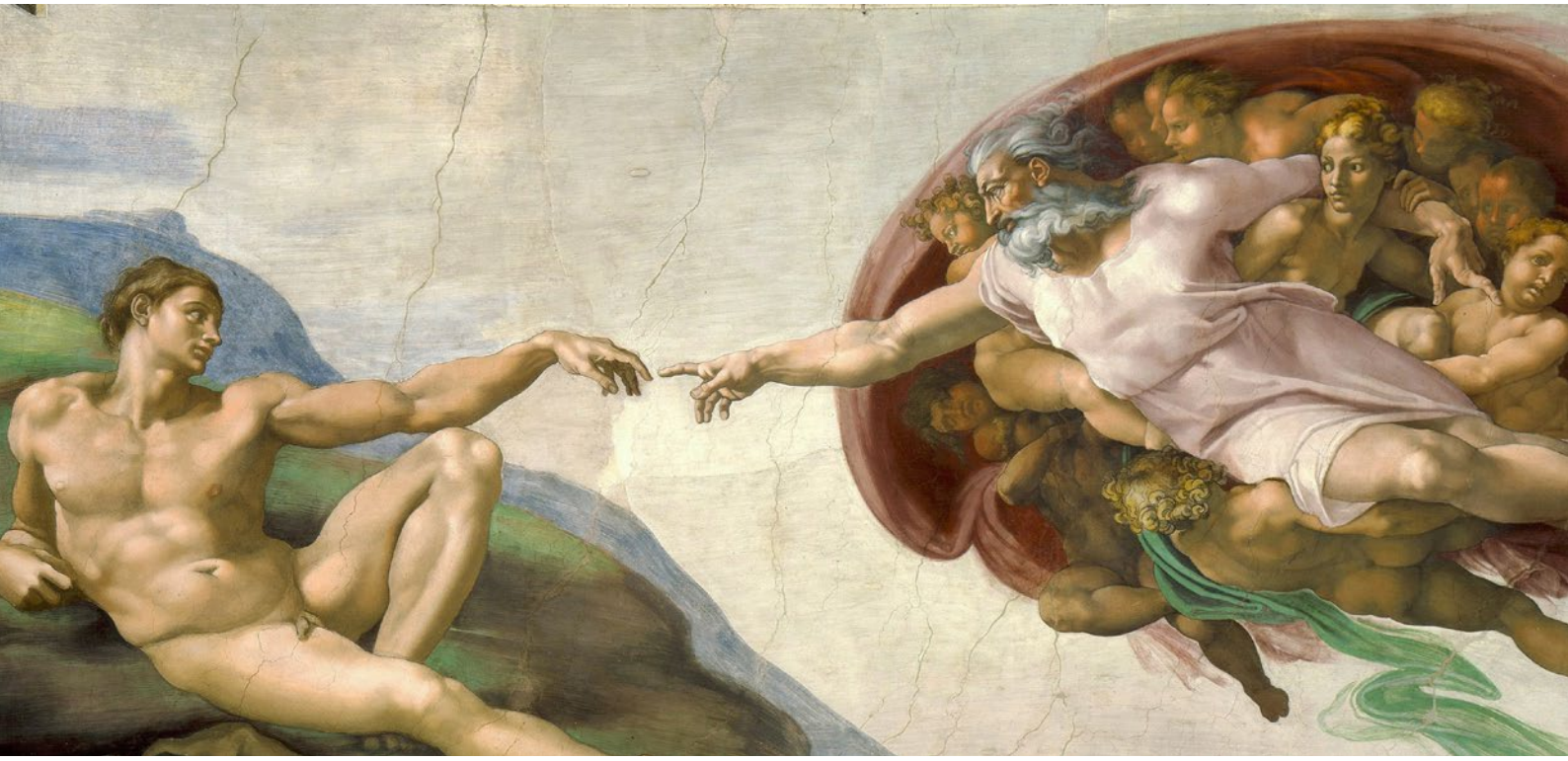
The crystal structure is of just one type of HLA called HLA-A*11:01, which is common amongst Chinese and the most common type in Singaporeans. In the next three to five years, the team hopes to solve the structures of all other HLA molecules that are common in Asians.

Prof Vathsala described the project as a serendipitous collaboration of basic science and clinical research to solve a longstanding problem in the clinic. "We [at NUH] have a wonderful campus in our backyard where we can meet with experts from Microbiology and Immunology. The project grew out of a chance tea where Paul and I met and said, 'Let's solve this problem and look at the structural aspects of antibody and antigen.'"



OPENING PANDORA'S BOX

Chinese scientist He Jiankui stunned the world when he announced that he had successfully edited the genes of two new-born babies. Is gene editing technology safe? What are the implications of manipulating the human genome? Associate Professor Roger Foo, Senior Consultant at the Cardiovascular Research Institute, National University Heart Centre and Dr Owen Schaefer of the Centre for Biomedical Ethics share their perspectives.



AN ETHICAL DILEMMA

It is no longer unusual for the young today (i.e. medical students) to have a vast and worldly travel experiences. Walking along a corridor at Heathrow Terminal 5 last year (alas some of us still travel by British Airways), I came across an advertisement meant absolutely to capture the attention of the passing public (see figure). For a while now in the UK, there has been growing concern that covert slavery is festering in the "underworld" up and down the country.

I guess we should excuse the advert for stereotyping the characters with Asian faces. But this advert struck me. Five years ago, upon returning to Singapore to work, my ageing dad fell seriously ill, and for the first time, our family had to employ a helper. One evening that week, I found myself waiting at the arrival hall of Changi Airport, and saw a frightened trembling young girl (our new helper) walking out of the baggage claim area. Beside her was the "maid-agent" who had accompanied her from her homeland. How are these scenarios different, apart from the country and the context? The issue of perspective always strikes me very hard, as it must do for those of us who keep aware of the larger changing world around us.

Last year in November (2018), a scientist (Dr He Jiankui) in Shenzhen proclaimed that he had successfully brought 2 CRISPR genome-edited babies into the world[1]. Lulu and Nana were allegedly new-born to a couple whose father has HIV, but unlike all other foregoing IVF conceptions in past decades, Dr He had edited the CCR5 gene in the embryos so that both babies have been born with CCR5-deficiency. Individuals with CCR5-deficiency are resistant to HIV[2].

Dr He made his first announcement on YouTube[3], fortuitously before an International Genome Editing Summit in Hong Kong. The disclosure provoked international outcry[4]. Scientists in the field condemned He's actions. Professor Feng Zhang (MIT), one of the inventors of the CRISPR-editing technology, called for a moratorium on the use of CRISPR to create gene-edited babies. At the Summit, Dr He presented and defended his work saying "I feel proud"[5].

Rumours abound. No one has yet said that they have seen the babies. A second gene-edited pregnancy is apparently under way. The Chinese government has since suspended He's research activities. Aligning with the international furore, the authorities have denounced the research as "extremely abominable in nature" and in violation of Chinese laws and science ethics[6]. The Chinese state media confirms the existence of the two babies, but the research was apparently not officially funded, and the state was not made aware previously. Dr He's whereabouts are now uncertain. Some on-going investigations include "collaborators" of Dr He from esteemed institutions in the West, including his former mentors.

Without revisiting countless well thought-out reviews and ethical debates on the matter, some prominent points are worth mentioning. (1) CRISPR is not yet deemed safe for human use. There are scientists in the HK summit who noticed serious off-target effects from his CRISPR-edited gene sequences. (2) Dr He did not get bona fide consent from the parents. He consented the procedure

as a vaccination to prevent HIV in the babies. Arguably, he would claim, his non-expert patients (the parents of Lulu and Nana) would not have easily understood the difference between the two approaches. The onus is on the scientist to ensure a clear understanding. (3) Dr He had failed to get an ethical board approval from his own institution, and went instead to another institution and obtained approval to proceed. Yes. There actually was an ethical review board in the country which approved this research.

But Dr He earnestly believed himself to be doing good. Watch the video and note his sincerity. He may have been seeking fame and glory, but it is not hard to see that he really did think that he was pushing progress for mankind. Note: pushing the progress is also what we urgently want to do here in Singapore. Dr He actually went to the lay public and sought open opinion before embarking on his project: "would you want to have a gene-edited baby where a disease is prevented", "what if there is some risk", "is HIV a disease worth preventing". Maybe unsurprisingly, He received significant majority support from his public. Still, it seems wrong for Dr He not to articulate the serious risks of the procedure. Or was he aware of the serious risks himself? Had he assessed the risks and thought them to be low and worth taking?

What about when the risk is one day removed? When gene-editing is perfectly razor sharp, and we no longer have to worry about complications of off-target editing or mosaicism from incomplete cell targeting. Does that then become ethically acceptable for us to proceed with gene-editing our babies? When the risk-benefit argument becomes less relevant, we will be pushed to consider whether editing to treat a baby's disease, or editing to augment a baby's trait, is acceptable. Debate that human augmentation should never be approved rages: editing to improve brains or looks, does not sound ethical on so many levels. But this presents a very slippery slope. Are we not merrily augmenting ourselves through the countless aesthetic clinics at shopping malls all across our island nation? If you have the precise tool to secure an intelligent, healthy and good-looking baby, what is there to stop you racing to the front of that queue?

The world has actually been here before. A lesser-known cousin of Charles Darwin was Francis Galton, who allegedly never got over the spotlight and pride of place his cousin enjoyed. Galton believed he had found the perfect "translation" for Darwin's science by acting on the question, if nature "achieves such remarkable effect on animal populations through survival and selection", why can't we accelerate the process by human intervention?

Thus, the science of Eugenics was born. Galton went about curating evidence that beauty, and even behaviour, were distributed in bell-shaped curves. In pedigrees of eminent men, 1 in 6 of all accomplished men are apparently related. One in 12 sons of eminent men go on to eminence, whereas by random selection it is merely 1 in 3000. Hence, like the breeding of horses and hounds even today, Galton advocated for "Selective Breeding". The good-looking should marry the good-looking, etc. In the USA, Dr Charles Davenport (1866-1944) went further to advocate for and establish colonies to house the "genetically unfit". The operational effort grew in many states to eliminate "defective strains" in America.

Unsurprisingly, colonies started carrying out Selective Sterilisation in those deemed genetically unfit. These were all mainstream. Experts met at international congresses for Eugenics. Professorship Chairs of Eugenics were established. In Germany, this became called "racial hygiene". And before long, the world entered the abyss of Selective Termination: removing the "lesser race" and "less genetically pure". The people carrying out these procedures were seriously sincere in doing good. Richard and Lina Kretschmar, ardent supporters of the Nazi regime, petitioned Hitler to euthanize their 11 month old son Gerhard because he was born blind and with deformed limbs. They believed they were serving their nation by eliminating their child from the nation's heritage.

Admittedly, my examples here risk plagiarising from Dr Siddhartha Mukherjee's book[7]. He has written eloquently on mankind's journey of the Genetic Discovery. It is a must read that delves into the topic.

We are in exciting times in science and medicine. It really is possible to sequence a person's whole genome at a very affordable price today. My relatives and patients ask me everyday: why sequence the genome if there is nothing you can do to correct it. But, the means to edit/correct a genome has also become very accessible (at least in the lab for now). This is the democratisation of science today. No longer is technology only within the reach of the richest one or two labs or countries in the world. Any lab worth its funds can buy CRISPR tools and use them readily.

In our lab, we edit a gene nearly every other month. We can not only edit/correct genomes, some labs are writing genomes (constructing organisms). When man can read genomes on the one hand, and edit or write them on the other hand, is this when he becomes God? Will we recognise an ethical dilemma when we see one?

Assoc Prof Roger Foo

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A CASE AGAINST A MORATORIUM ON GERMLINE GENE EDITING

Should researchers put the brakes on genetically engineering babies? Leading scientists and ethicists recently called for a moratorium on clinical applications of germline gene editing: inheritable alterations to the DNA of embryos to improve kids' health or other features – or just "gene editing," for short.

This declaration was prompted in part by the birth last year of the first gene-edited babies in China. The birth was roundly condemned by experts and may result in charges against He Jiankui, the lead scientist involved.

The call for a moratorium is grounded in two main concerns. Its supporters assert, first, that the risks of gene editing are simply too uncertain and potentially large to proceed. Secondly, the deeply controversial nature and potential social impact of altering human DNA means researchers need "broad societal consensus" before proceeding.

The authors suggest a five-year pause to wait for more scientific progress and public dialogue. At that point, the authors propose, societies may choose to begin a path forward for gene editing, if risks are deemed acceptable and the process is fully transparent.

However, several scientists have pushed back against the call for a moratorium, including gene-editing pioneer Jennifer Doudna and geneticist George Church. As a biomedical ethicist, I believe the objectors raise valid concerns about the relevance and usefulness of a moratorium that are worth reflecting upon.

Plenty everyone agrees on

To be sure, those for and against a moratorium actually agree on some key points.

Almost no one thinks the world is ready for clinical trials today, as more basic science is needed to minimise risks like editing the wrong bits of DNA, or "mosaicism," where some but not all DNA in an embryo is altered. He Jiankui's rogue science was clearly unethical for this and other reasons, including a lack of transparency and flaws in informed consent.

There is also no pushback against the idea that the world needs to have a public conversation about gene editing. Do you want to live in a society where embryos' DNA is edited in order to improve the lives of the next generation? Are the risks of gene editing worth the benefits? Can and should we draw a bright line between editing for disease prevention and editing for enhancement? These questions cannot be answered only by experts, and require substantial public engagement.

Nevertheless, a divide over other issues remains.

Moratorium redundant where laws already exist

Already, over 30 countries prohibit this sort of gene editing, either by law, regulation or enforceable guidelines. For this reason, it was quite easy for the director of the U.S. National Institutes of Health to endorse the proposed moratorium – vthe NIH, the largest public funder of biomedical research in the world, is already prohibited by law from funding clinical

applications of gene editing. So a moratorium is at best redundant in those nations, perpetuating the status quo.

It is also liable to cause confusion. If a country or scientific body announces a moratorium as recommended, this could misleadingly imply that germline editing was previously permitted and unregulated. It could also suggest that some countries' bans will expire in five years, when currently none has a time-limited prohibition.

Arbitrariness of a blunt instrument

At the same time, I believe a moratorium could work in countries that currently lack prohibitions on gene editing. It could help prevent rogue scientists from seeking environments that are relatively unregulated to pursue dubious experiments. This is what happened with the first births using mitochondrial replacement (so-called "3-parent IVF"): An American fertility doctor carried out part of the procedure in Mexico because he perceived the rules as laxer there.

Additionally, the call can be heard as an argument for reform of current laws and regulations: Society should revisit prohibitions and – depending on the evidence and popular opinion – consider rescinding them in five years' time.

But some researchers remain concerned that a moratorium is an overly crude and arbitrary means of regulating a controversial new technology. While the technology is currently not fit for clinical use, are scientists so certain that it still won't be within five years' time? More flexible regulatory frameworks that do not include arbitrary timelines could better adapt to rapid scientific developments and shifts in public perceptions.

A call for public input – without public input

Finally, it's unclear whether a moratorium is consistent with the democratic norms that the proponents of a moratorium espouse. In particular, they reiterate the idea that researchers should only proceed with germline gene editing if there is broad societal consensus on how to proceed.

But shouldn't a moratorium itself be subject to the requirement of broad societal consensus? Blanket prohibitions will have a substantial impact not just on the scientific community but on access for the rest of society to the potential fruits of research – a potential infringement of the human right to benefit from science. Whether that infringement is justified is an important question that cannot be answered by experts alone.

To some extent, democratic countries that ban gene editing will have already undergone typical (if flawed) democratic processes to come to that decision. But in places that the moratorium is not redundant, it is reasonable to demand broad societal consensus before proceeding with a moratorium that even leading scientists don't all agree on.

The cautious may argue that a presumption against gene editing is warranted before consensus can be established, because of the substantial individual risks and societal impact of proceeding to alter the human genome for future generations. However, those societal risks are very substantial only if gene editing quickly becomes widespread. That is something careful regulation rather than a blanket prohibition might be well-suited to address.

In addition, I see it as somewhat problematic for experts to impose their own personal assessment of whether the risks outweigh the benefits of gene editing on the rest of society. Weighing risks and benefits is a fundamentally ethical issue, not one where scientific expertise can resolve the matter.

In the end, though, there seems to be broad agreement on the need for greater public deliberation over the questions related to germline gene editing: on whether gene editing is permissible, on whether a moratorium is appropriate – and more fundamentally, on what sort of a society we all want to live in.

Dr Owen Schaefer

This article was originally published in The Conversation on 20 March 2019.

INSIGHTS

You can shed tears that she is gone,
or you can smile because she has lived.
You can close your eyes and pray that she'll come back,
or you can open your eyes and see all she's left.
Your heart can be empty because you can't see her,
or you can be full of the love you shared.
You can turn your back on tomorrow and live yesterday,
or you can be happy for tomorrow because of yesterday.
You can remember her only that she is gone,
or you can cherish her memory and let it live on.
You can cry and close your mind,
be empty and turn your back.
Or you can do what she'd want:
smile, open your eyes, love and go on.

From "Remember Me" by David Harkins (1982)

LIVING WITH LOSS: A WORD OF CONSOLATION TO 'THE ONES LEFT BEHIND'

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

As I write this, Singapore is mourning the death of one of her young sons, who lost his life in the line of duty. 28-year-old actor Aloysius Pang was seriously injured while on military reservist training in New Zealand and died a few days later. His funeral was held on 27 January 2019 but it will be far from over for his family and friends, the SAF and, judging by the social media buzz, anyone with an opinion on the matter.

To most of us, this would be another example of how fragile life can be, and the suddenness of the loss, the manner of it, can be as traumatic as the loss itself. No chance to say good byes, no opportunity to say anything at all.

Birth and death are universal human conditions, yet ironically, each of us will experience these phenomena, directly and indirectly, in our unique way. So we can never really say "I know how you feel", because we do and we don't, at the same time. Many of us, as we get older, will lose not only ageing parents but also contemporaries.

Recently, at the close of 2018, a classmate of mine died in a hospice and when the news circulated around our WhatsApp chat group, people started to reminisce about her and about others who had passed on at a young age. The youngest was a Primary 6 classmate, G. She broke her arm during basketball one day and ended up having her right arm amputated for bone cancer.

I remember telling my father about it, and in his typical blunt way – remember I was 11 years old – he told me it would spread to her lungs and she would die. I was furious

with him, but of course he was proven right. Back in those days, there was effectively no other treatment, and the disease was pretty much lethal. G managed to return to class for a while, but inevitably, she started skipping days, and eventually stopped coming.

Someone shared that she had spent many hours playing her favourite game "Othello" with G on the days that she was well enough to attend class, and her death continued to affect her even in secondary school. What I recalled was being told that the night before G died, she told her mother, "Don't cry mummy, the angels are coming."

As the stories above illustrate, the person does not have to be our relative for us to be affected by his or her death. And that effect can go on for months or even years; I can still picture G with her gentle nature and sunny smile, wearing the floral poncho her mum made to make the amputation less obvious.

First, a few definitions:

Grief is the response to loss, and has several dimensions – emotional of course, but also physical and cognitive.

Bereavement is the state of grieving and mourning that follows the death of a loved one, or any significant other (including pets).

Mourning refers to the rituals or expressions of loss e.g. funerals, memorials, wearing black etc. These rituals have important social signaling functions, announcing to the community that the family was in a state of adjusting to the new status quo.

I will not dwell on the theories or models of grief, nor on the process of grieving. Those who are interested to learn more can refer to the Singapore Hospice Council booklet "Caring For Yourself and Others After a Death" *(https://www.singaporehospice.org.sg/en/wp-content/uploads/2018/10/Caringforyourselfandothers-web.pdf)*

What I will say, however, is that the impact can hit you like a sucker punch, even when you thought you were mentally prepared. For some, the loss is total, practically the end of the world, like W.H. Auden had written in "Funeral Blues":

He was my North, my South, my East and West,
My working week and my Sunday rest,
My noon, my midnight, my talk, my song;
I thought that love would last forever: I was wrong.

The stars are not wanted now; put out every one,
Pack up the moon and dismantle the sun,
Pour away the ocean and sweep up the wood;
For nothing now can ever come to any good.

For others, the ultimate cruelty is that rest of the world just

carries on, seemingly oblivious to the pain of the bereft:

"Lament" by Edna St Vincent Millay

Listen, children:
Your father is dead.
From his old coats
I'll make you little jackets;
I'll make you little trousers
From his old pants.
There'll be in his pockets
Things he used to put there,
Keys and pennies
Covered with tobacco;
Dan shall have the pennies
To save in his bank;
Anne shall have the keys
To make a pretty noise with.
Life must go on,
And the dead be forgotten;
Life must go on,
Though good men die;
Anne, eat your breakfast;
Dan, take your medicine;
Life must go on;

I forget just why. Whatever it is, do not let anyone tell you that you will get over it. It is not a matter of "getting over" this, it is more of a process of "going through" it, eventually emerging changed, but hopefully more or less intact. It is important to realise that everyone grieves differently, and these do not reflect differences in love and caring. And because it is a process, it will take time.

But don't take my word for it. Renowned grief expert William Worden, in his book "Grief Counselling and Grief Therapy", had suggested Four Tasks of Grieving. These are:

1) To accept the reality of the loss.
2) To work through the pain and grief.
3) To adjust to a changed life.
4) To "relocate the loss" i.e. maintain a connection with the deceased and move on with life.

Or, if you prefer, you can take the advice of the late American poet Mary Oliver (10 Sept 1935-17 Jan 2019):

"to live in this world

you must be able
to do three things
to love what is mortal;
to hold it

against your bones knowing
your own life depends on it;
and, when the time comes to let it go,
to let it go"

Resources:
http://singaporehospice.org.sg/bereavement/
http://singaporehospice.org.sg/community-bereavement-service-providers/

Noor Melati Ahmad, Nurse Clinician, National University Hospital, SARS survivor

SARS made me a better nurse

WHEN I started work as a nurse in 2001, after graduating from Nanyang Polytechnic, I never thought I would end up on the hospital bed as a patient. Two years later, it happened.

I got the Severe Acute Respiratory Syndrome (SARS) infection from a patient who had come to NUH for treatment. At 22 years of age, all my concerns then were about my family and my boyfriend. I was scared I may not see them again!

I had all the symptoms. The high fever, chills, body aches and shortness of breath which went on for weeks. It was an emotional rollercoaster. I felt isolated, lonely and afraid. I was hospitalised in Tan Tock Seng for three weeks and at the Communicable Diseases Centre for a week. Even though I could see people coming to work and going home from the window of my room, it still made me feel like I was in a prison.

For a person who enjoys being in contact with colleagues, patients, family and friends, being confined in a room for two weeks was hard. Even the nurses, wearing full protective gear, would spend very little time in the room. They would only come in to give me my medicine and food.

Noor Melati Ahmad (centre) with NUH colleagues who gave her support during her SARS ordeal.

I was allowed to have my phone and talked to my loved ones very often during this difficult period. My mother would call me every day and each time we talked, she would cry. Even my father, with whom I had a very strained relationship at the time, became emotional. I felt I had to put aside our differences and told him: "I am sick and I do not know if I will come out of this. I just wanted to say I love you." And he replied in Malay: "Ayah pun sayang Noor (father loves you too, Noor)." That is probably the only time he has ever said that to me.

After I was given the all-clear from SARS, my grandmother asked my mother to stop me from continuing with nursing. She felt I had escaped one infectious disease but may not be so lucky the next time. My mum stood up for me. She told my grandmother that my SARS episode was a sign that I could overcome any ordeal.

It helped that nurses were in the limelight at that time, so my mum motivated me to continue to help others. The SARS ordeal strengthened my relationship with my boyfriend too. We got engaged in 2004 and married a year later, after I finished my advanced diploma in nursing focusing on oncology. Now we have two daughters and a son.

SARS taught me that life is short, that we must appreciate what we have. As a nurse, you see caregivers and patients at their most vulnerable. I see death almost every day and I have patients who are so young, university or polytechnic age, or young mothers diagnosed with breast cancer or leukaemia.

I remember what I felt like as a SARS patient and try to spend as much time as I can with them, talking to them about how they feel. They ask me: "Am I going to die?". It is hard for them to hear that they have cancer and, in some cases, they might not recover from it. But when they accept it, they appreciate the time they have to spend with their families.

"Caring for our People: 50 years of healthcare in Singapore"; reprinted with the kind permission of MOH Holdings Pte Ltd.

Family affair - NUHS primary care staff at the Department of Family Medicine's inaugural Strategic Planning Retreat on 16 January 2019.

BUILDING FAMILY MEDICINE AT NUS/NUHS: A PROGRESS UPDATE

By Professor Doris Young,
Head, Department of Family Medicine,
National University Health System

The Department of Family Medicine (DFM) at NUHS was established on 1 Feb 2018. Much work has been done, including appointing new department and education managers and consolidating the Undergraduate Family Medicine curriculum to extend it across four of the five years of the MBBS at the NUS Yong Loo Lin School of Medicine.

Some new initiatives proposed in the Undergraduate curriculum extended student learnings in public health principles to practice experience in the community and introduce primary care research to students undertaking FM selective.

In first year, we have introduced the Longitudinal Patient Experience, care giver experience with nurses (Inter-Professional Education) and expanding the Family Medicine presence in Phase III. This includes a foundation week to introduce the essential attitudes, skills and knowledge of Family Medicine. In addition, three weeks of a FM selective in phase IV has been offered to 30 students.

NUHS Family medicine residents' numbers for 2018/9 is now 21. This is almost double that of previous years and in July 2019, we will have 30 first year residents joining us. Thus, with National University Polyclinics (NUP) coming on board as a strong partner, we are well on our way to provide the best diverse experience for our NUHS residents, in partnership and collaboration with the Jurong Community Hospital in addition to our existing valued partners at NUH, St Luke's, Raffles Medical Group, as well as the Frontier Family Medicine clinics. We are also identifying new career pathways (academic registrars) for young Family Physicians to take up academic careers in teaching and research in addition to their clinical training, post Masters of Medicine/Fellowship in Family Medicine. In research, the Primary Care Research Unit (PCRU) has been established and we are now actively recruiting research staff to help build research capacity in Family

ALL IN THE FAMILY

Medicine and Primary Care. The PCRU will provide research support to NUP and other disciplines at NUHS to conduct research that improves health practices and patient outcomes. A multidisciplinary advisory group will help to guide the Unit on innovation research themes, methodologies and funding sources.

Work is also on-going with the Regional Health Service to engage primary care networks (PCN) GPs to take up the challenge of not only providing acute care to patients, and also care for the elderly with chronic diseases such as diabetes and high blood pressure and ensure they receive the best treatment.

Six strategic goals to challenge and inspire our efforts

To map the way forward, the Department held its inaugural Strategic Planning Retreat on 16 January 2019 with key leaders and practitioners from the NUH, Yong Loo Lin School of Medicine and the National University Health System (NUHS) primary care entities.

Participants were given progress updates: The three key areas that the Department would be focusing on in the short and medium terms, between now and 2020 are Education; Research and Clinical Services. The Department would initiate and drive these areas under the NUHS umbrella and expand the academic standing of Family Medicine, through education and research, and producing high quality clinical outcomes, for our community.

Working closely with key strategic partners and stakeholders the Department of FM staff identified six specific goals:

1. Quality People: identify and nurture the best talents locally and internationally in FM education and primary care research

2. Quality Research: recruit and expand the research unit (PCRU) in collaboration with key partners and stakeholders to establish NUHS Family Medicine as a key contributor to innovative medical and health services research

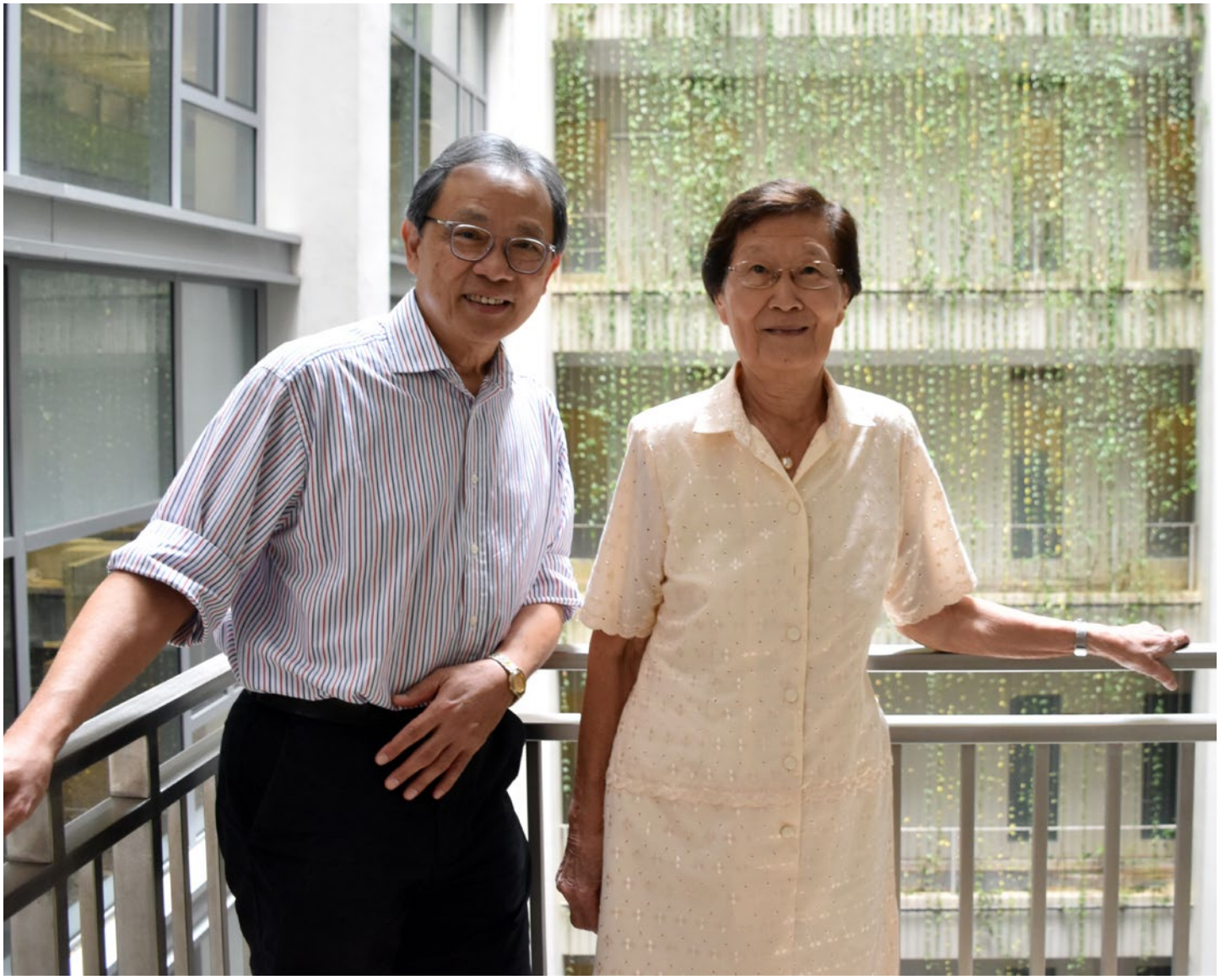
3. Quality teaching & Learning: provide high quality teaching and learning platforms for medical students and residents in Family Medicine

4. International Positioning: align with the Yong Loo Lin School of Medicine's high international ranking by benchmarking Family Medicine at NUHS with other high performing Departments of FM

5. Strengthening Community Care Relations: partner key stakeholders to provide comprehensive and quality patient care to the community

6. Quality Management: ensure continuous improvement and best practices in the Department

Moving forward, the future of the Department of FM at NUHS is exciting and dynamic as we will address the three beyonds stipulated by Ministry of Health: 'moving hospital care to the community, health care to health and quality to value' through FM education, research and supporting our partners in the wider community.



Teacher and her student - Dr Wong Hee Ong with Professor Kua Ee Heok.

THE THREE H'S OF MEDICINE

Medical technology has advanced by leaps and bounds, but the ethos of medical practice remain constant.

Alumna Dr Wong Hee Ong, who graduated from the University of Malaya, Singapore (former King Edward VII College of Medicine) in 1953, and subsequently taught in the Faculty of Medicine, University of Malaya (UM), Kuala Lumpur believes that all doctors should be guided by the 3Hs in the practice of medicine - using their heads, hands and hearts.

The practice of medicine has become technology-driven and many doctors and medical students today tend not to use their senses adequately when they see patients, she asserts. The art of medicine is gradually being overshadowed by technology.

"As students, we were taught to notice how our patients walk and smile, for clues to their diagnosis. I think of Sherlock Holmes: we were taught to use our eyes, ears, hands to examine patients, and to talk to our patients, because very often the patient is telling you the diagnosis. This was also the basis of how we taught our students, which is more educational than didactic lectures", said Dr Wong, who was Professor of Medicine, UM and Consultant Physician in Kuala Lumpur. Once, she attended to a patient who had weakness in her leg. She asked the woman for more details, examined her, and concluded that she had a brain tumour. Months later, the patient visited her again and said she indeed had a tumour, which was removed in Singapore. The patient admitted that she did not believe the diagnosis and wondered what the brain had to do with the leg. Dr Wong then realised that she should have spent more time to explain to the patient.

"You need to let your patients have the confidence. It is worthwhile spending time to talk to your patients to get a detailed history of their symptoms, examine them

Dr Wong Hee Ong (front row, second from left) and her classmates from King Edward VII College of Medicine at a reunion event in 1997.

carefully so that you get the right provisional diagnosis. Then order the correct tests to confirm your diagnosis. This will save your patients from having unnecessary tests or taking unnecessary medicines, thus helping to keep healthcare costs down. A good doctor should be empathetic, treating the patient as a whole person, and be aware of the circumstances he is in – the family situation, social economic status – which could relate to his illness. In other words, practise with your head, hands and heart."

Life in early 1900s

Born in Singapore in 1927, Dr Wong was the fifth child in a family of 10 children.

She was in secondary school when World War II disrupted her studies.

"There were bombs everywhere. I fell ill and almost died, but I recovered," she said.

At age 14, Dr Wong worked as a cashier in a doctor's pharmacy. As her wages were meagre, she went from one job to another, learnt the Japanese language and learnt how to operate a Japanese typewriter, which was large and cumbersome. She ended up working for a big Japanese firm typing letters in the Japanese language for the Manager.

After the war ended, she returned to school in 1946 and qualified for medical school at age 19.

"In those days, there were very few career choices - becoming a doctor, a teacher, a nurse or a pharmacist. Since my brother was already in medical school, and all my friends wanted to do medicine, I followed and applied."

She was one of three Singaporean girls in her cohort of 80, each selected from the top three girls' school in Singapore. The remaining seven girls came from Malaya.

A career in teaching and clinical work

Upon graduation in 1953, Dr Wong worked as a medical officer, caring for patients at the general ward of the Singapore General Hospital. She also mentored medical

Dr Wong Hee Ong (front row, sixth from left) and her King Edward VII College of Medicine classmates.

students who visited the ward for their practical bedside studies, and taught them how to deduce the patient's diagnosis by taking a good history, using their eyes, hands, and thinking logically.

In 1964, the University of Malaya in Singapore decided to set up the Faculty of Medicine in the campus in Kuala Lumpur (KL), and Dr Wong and a few others were sent to help establish the Faculty and the new University Hospital in KL. Singapore separated from Malaysia in 1965 but Dr Wong stayed on in KL.

She joined the University of Malaya's Faculty of Medicine as an associate professor and later became Professor of Medicine and Consultant Physician to the University Hospital. She retired in 1978 after having taught 14 batches of students. Among Dr Wong's students are psychiatrist Professor Kua Ee Heok and gynaecologist-obstetrician Professor P C Wong, both with the NUH.

"Every time I see my students' achievements, I feel so happy. As the saying goes I 'bask in reflected glory'. My happiest moments are to see my students do well. So many of them are professors now," said Dr Wong, who after retirement went into private practice as a consultant physician and cardiologist in Kuala Lumpur.

In 1992, she was offered the post of Chief Executive Officer to establish Gleneagles Hospital in Kuala Lumpur. The hospital had to be planned and built from the ground. It was a tremendous responsibility but very satisfying as "I learnt a lot about planning a user friendly hospital and all the safety features that should be incorporated into a hospital building". She later became a Chief Surveyor, on a voluntary basis, for the Malaysian Society of Quality in Health to train hospital staff and accredit hospitals for the Society which is a member of the International Society for Quality in Health.

Active ageing

Dr Wong returned to Singapore in 2010. She attends Chinese classes and lectures as part of lifelong learning and also takes part in the dementia prevention programme called Age Well Every Day, which is run by the National University of Singapore's Mind-Science Centre.

As part of the programme, Dr Wong trains volunteers to give dementia-related health talks to seniors at various centres in the community. The programme also has music and art therapy, and gardening, as well as mindfulness practice and exercise sessions for seniors.

"Getting involved in this dementia prevention programme helps me from developing dementia. It is good to find something satisfying to do, and have social interaction with others."

MUSIC HELPS HER BE A BETTER DOCTOR

Out of pain and heartbreak come songs of hope and renewal.

Stephanie (second from right) and her classmates on campus.

In August 2014, when her 78-year-old maternal grandfather suffered heart failure and was rushed to the National University Hospital's Emergency Department, then-Phase 1 Medicine student Stephanie Yeap felt compelled to pen a song about the entire experience.

"That moment was very poignant and very painful for me, so I wrote it into a song called 'Emergency Room'. I detailed how I perceived my grandfather as a child, and how I looked up to him so much, and how sad I was to bid him goodbye at the Emergency Department," she said.

The following year, Stephanie took part in a student project to raise public awareness on palliative care. She was responsible for the project's publicity video, and proposed a song to accompany the video.

"I was quite inspired by the whole movement and the many whimsical answers people wrote about what they wanted to do before they died, on the 'Before I Die' boards put up in the public areas. Some of these responses include wanting to see Leonardo DiCaprio win an Oscar, finding true love and getting married, and travelling with loved ones," said Stephanie, who spent close to a month composing both the song and the accompanying lyrics.

"They were very whimsical and silly compared to those written by those who were terminally ill in the hospices. A lot of their wishes were to spend time with family and friends before they passed on. A lot of their messages were also telling people to treasure what they have on earth now. I was very inspired by the contrasting messages, which is why the song I composed was very whimsical at the start, though it ended thoughtfully."

To encourage her schoolmates to persevere in their studies and be compassionate and socially responsible doctors, the Medical Society Arts and Cultural Directorate member also co-wrote and performed a song titled, "Ours to Build". The song, which was performed at the Freshman Orientation Camp in 2017, as well as the White Coat Ceremony in 2018, was very well-received by the audience.

Beginnings

Her love for music and song writing began in childhood.

She learnt classical piano at four and enjoyed writing poems in primary school.

"I didn't have a lot of pop music influences, because my parents made me listen to classical music most of the time. So when I was introduced to Avril Lavigne, my songs sounded very much like hers," Stephanie said.

When Stephanie was in junior college, she joined her school's rock band as a keyboardist. Her ad hoc coaches

noticed that she had good vocals, and made her lead singer. She also learned to play the guitar a few months before their public performance.

Post junior college, she submitted two original songs – a whimsical love song from her college days, and 'Emergency Room' – to the National Arts Council in a bid to join the seven-month long music mentorship programme called Noise Singapore.

Touched by the raw, heartfelt emotions in her songs, 98.7FM deejay and former Lush 99.5FM programme director Vandetta taught her to improve her song writing skills and her stage presence.

"That whole experience was fun, because I managed to do gigs in a lot of places on my bucket list, such as Timbre Substation, Esplanade Concourse and even live on Lush 99.5FM. It's very exciting for someone who first forayed into music and getting all these gig opportunities. I think it was very good for me in the sense that not only did it grow me as a musician, but it helped me link up with a lot of other professional musicians and I got a lot more gig opportunities after this," she said.

Maturing

Initially awkward on stage, Stephanie is now a seasoned performer who can rally her audience.

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"As a performer, I have matured in the sense that I am a lot more comfortable with crowds now. I used to be very awkward and super bad with stage banter. I also recognise that different settings will have different audience responses, so I learnt to mediate my expectations of the audiences as well," she said.

Over time, the themes, song arrangement and chords for Stephanie's songs have also become more complex.

"I always try to make my music a bit different from the usual love tracks, but over time I have also learnt to be more honest with myself in song writing. I realised sometimes it was okay to be raw about your emotions, especially following heartbreak or being in love. It was important for me to acknowledge these feelings."

Marrying music and medicine

Now, Stephanie – who goes by the name Stephycube – is preparing to launch her Extended Play (EP) on Spotify in

Stephanie performing at an event.

July. She has already launched two singles, titled 'Departure' and 'Most of All' this year.

"One important mission I had with my EP was to prove to people that your day job doesn't define who you are. Your passions are what really define you. I am a musician and a future doctor, and I think there is an important message that I want to share with people. Previously, some people used to think if you did arts, you should stay in arts, and vice versa for the sciences. But if you have a passion for music, you should go for it and pursue your dreams," she said.

When Stephanie was attached to the Institute of Mental Health, she met a boy whose parents said he could not pursue his love of music. She seized the opportunity to encourage him to press on with his passion.

"Music itself has allowed me to become more empathetic towards patients. I encouraged him to chase his passion, and told him that it is not impossible for him to do music and something else at the same time. I think he was quite encouraged by that." She walks her talk as a member of the National University Centre for Organ Transplantation's (NUCOT) band, which is made up of organ transplant patients and doctors. It performs regularly at fund raising events.

"Music helped me connect with a lot of people because it is a universal language. It brings the humanity out of patients a lot more. I think a lot of doctors tend to forget about that sometimes when they practise. It is also a very good way to reach out to fellow doctors interested in music making. Music has changed my medical school journey a lot."

Gleanings

She has two tips to offer budding musicians.

"Don't be afraid to try whatever gig opportunities you can get, whether they are small or big events. Everyone starts somewhere. I think a lot of people limit themselves because of their own expectations of who they want to be as artistes.

"Don't be too hard on yourself if the first few gigs don't go too well, or if you find the audience response lacklustre. You would find that even after performing for some time, the audience response could still be very lacklustre, and it's not your fault. So it is more important to improve your craft in terms of vocal and music ability, and song writing."

Watch Stephanie's music journey at Youtube.com

MAY
JUNE
JULY

27 May
14th NUS-Nagasaki Symposium
LT35, Level 1, Centre for Translational Medicine (MD6), NUS

13 June
ASEAN Simulation User Network (SUN) Meeting 2019
Level 3, Centre for Healthcare Simulation, Centre for Translational Medicine (MD 6), NUS

03 July
Medical Dinner 2019
Padang & Collyer Ballrooms, Raffles City Convention Centre

14 July
Commencement Ceremony
University Cultural Centre, NUS

26 July
NUS Medicine Awards Ceremony
Auditorium, Level 1, NUHS Tower Block

Details are subject to change.

Inspiring Health For All

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School of Medicine