01 Issue
April 2015

2015 marks Duke-NUS' 10th Anniversary and also a new chapter for the school with Prof. Thomas Coffman (right) taking over the reins from Dean Ranga Krishnan (left) as Dean

PASSING THE BATON

With seven years as Duke-NUS Dean under his illustrious belt, Professor Ranga Krishnan is passing the mantle over to another distinguished research peer, Professor Thomas Coffman. Dr. Coffman, the current Dean-designate, will succeed Dean Krishnan when the latter's term officially ends on 30 June 2015.

Dean Ranga Krishnan

A Legacy of Partnership

Dean Krishnan – whose legacy of forging deep ties between Duke Medicine, NUS and SingHealth even as he contributed to R&D (Research and Development) and educational leadership in Singapore – expressed satisfaction for his tenure as Dean. "It has been great for me, a wonderful adventure. I took on the challenge because it was a once in a lifetime chance to build a medical school," he recalled. "It was a chance to start from scratch – in the absence of 'legacy' – and do new things to see if it worked. Not only did things proceed smoothly, we achieved all our key indicators ahead of time and budget, and we are on track to reach Phase III ahead of schedule."

Acknowledging that there was some scepticism about the venture in its initial days, Dean Krishnan said, "I questioned if Singapore was the right fit and if I could make it work, but I knew Singapore needed another medical school and that Duke-NUS had a chance to work with SingHealth to build a vibrant and pioneering academic medical centre that could transform medical care in Asia." This goal, to build academic medicine in Singapore, has proved successful as evidenced by the numerous collaborations with the various research institutions across the healthcare and research landscape, he added.

Taking Academic Medicine Further

And it is in this area of academic medicine that incoming Dean, Dr. Coffman, also hopes to take further. Dr. Coffman, a recognised leader in the field of nephrology, voiced his

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own excitement about the role and the chance to build on the strong foundation laid by Dean Krishnan. As founder and Director of Duke-NUS' Cardiovascular & Metabolic Disorders Programme, Dr. Coffman is no stranger to the school's work and achievements. As Dean, he will transition to a full-time position in Singapore and work towards raising the bar in medical education and enhancing research collaborations.

He said, "The goal – and biggest challenge – over the next five years is further develop Duke-NUS' partnership with SingHealth and develop systems to enable the pursuit of academic medicine in Singapore. We want to dovetail clinical work, research and education so that clinicians can more easily participate in research or teaching programmes and can integrate these aspects into day-to-day clinical practice. This will allow us to really bring our programmes to long-term fruition to influence patient care."

With the frameworks already in place, Dr. Coffman is looking to "flesh" out and build greater synergy between Duke-NUS and its partners. "Dean Krishnan has been a real visionary and established the framework, structures, and key players. I'll benefit from his work and will continue to manage and build on these as we move forward."

Coming from a more clinical background, Dr. Coffman hopes to bring different skillset to the table, that of improving healthcare delivery. "Leveraging the partnerships already forged, the goal is to bring Duke-NUS health researchers together with those in SingHealth to look at some of the issues of care delivery and patterns of care and figure out the best way to organise care. What we hope to do is catalyst positive change by capitalising on the superb clinical care that exists across the SingHealth system and the resources of the research programmes at Duke-NUS."

Prof. Thomas Coffman

Dean Ranga Krishnan (left) and Prof. Thomas Coffman (right) in front of the Duke-NUS Stone Wall.

Raising the Bar on Education

Over the next five years, Dr. Coffman aims to raise the education bar and produce students for the spectrum of medical work, from physicians and researchers to academics. "We aim to increase our intake from the current 60 to 75 students over the next five years," he shared. More than that, the aim is to ensure that graduating students return to pursue collaborations with Duke-NUS. "Our hope is that our graduating students, as those that understand both the clinical and academic sides, will form a new generation of physicians and researchers who can make fundamental changes in the way we deliver care," he said. This becomes even more pressing in an ageing population and with the rise of chronic disease.

The TeamLEAD approach, which has become a distinctive part of Duke-NUS education will play an important role in elevating medical education, said Dr. Coffman and Krishnan. "Here at Duke-NUS we have proved that team-based learning – a whole new paradigm in medical education – is effective and I am particularly proud that our innovative learning approach is now used at Duke in the U.S. not only in medicine but in other faculties as well," said Dr. Krishnan. In an era of user-based content, TeamLEAD is part of an evolving approach to learning, a focus on application, not memorisation of knowledge, he added.

The Duke-NUS Pioneers

DUKE-NUS: TEN YEARS OF GROWTH

Its glass and steel façade may form an iconic feature of the Outram campus today, but ten years ago in its fledgling days, research at Duke-NUS was represented by a five-foot space on a laboratory bench. Recalling its beginnings, Professor Pat Casey, Senior Vice Dean of Research and one of the founding members of the school, shared: "[My wife] Mei Wang-Casey, was Duke-NUS' very first clinician scientist and together we started the first laboratory. Even before Duke-NUS settled into its interim campus, Professor Kon Oi Lian of the National Cancer Centre Singapore was kind enough to loan us a five-foot bench to work at. That was where the Signature Research Programmes of Duke-NUS started."

Ambitious Beginnings

This humble beginning belies the school's ambitious vision – one that began with Drs. Casey and Dr. Mei Wang-Casey and, within six months, three other founding scientists from Durham's renowned Duke University. The goal was nothing short of being the top medical school in Asia and a premier research institution in the area of translational medicine. Dr. Casey said, "Mei and I thought it would be a good opportunity to move to Singapore to play a part in setting up Duke-NUS. It was a terribly exciting time, spending each day just tackling a long list of things to do. It was very much a start-up culture; everyone involved that first year just did what it took to get things going, whether it was meeting with senior officials from the government or academia, or cleaning up a storage room to get a little extra space before the interim facility renovations were completed."

The hard work has paid off, Dr. Casey said, looking back on the many milestones and achievements that now distinguish Duke-NUS as a leading medical education and research institution in Singapore and the region. " These achievements," said Dr. Casey, " include appointing the first research faculty, appointing the first Signature Research Programme director and having junior faculty develop vibrant Programme and go on to achieve international standing." The brand of Duke-NUS has also grown, he said. "Our recognition is quite good across Southeast Asia and even in the US. In fact, over 150 delegations from governments and universities throughout the world have come through to learn from Duke-NUS and its distinctive pedagogy - TeamLEAD. With such strong academic parents, Duke University and NUS, and SingHealth as our primary clinical partner, what we have is a convergence of cultures and stature that facilitates these accomplishments."

Going Beyond Expectations

"The school has surpassed my every expectation. I would not have predicted we would be the size we are today nor have the scope of activities we do," he said. While the medical school's yearly intake of 60 is still roughly within the size of what was projected, the reach of the school – through its collaborations in research and innovations in education – is extensive. "Our education programme now reaches into secondary schools in Singapore and back to Duke, impacting much more than the training of 60 medical students," he observed. "Our research programmes have become quite embedded in the fabric of the Singapore research landscape, with dozens of collaborations with major institutions like NUS, SingHealth, A*STAR and more. It has helped us achieve a critical mass that has made us greater than the sum of our parts."

"The school has surpassed my every expectation. I would not have predicted we would be the size we are today nor have the scope of activities we do."
-Prof. Patrick Casey

Prof. Patrick Casey (seated) and Asst. Prof. Mei-Wang-Casey (left) in a Duke-NUS lab in the early days

Dean Ranga Krishnan (third from left) and Prof. Patrick Casey (third from right) with colleagues during the school's topping up ceremony in 2008

A Culture of Partnerships

"These achievements could not have come about without the passion and innovative spirit of its researchers," said Dr. Casey. "Our basic and translational scientists all have a disease process that informs on their research projects. They are also all a little daring, they think outside the box and have a strong collaborative spirit. This means they engage the clinical community and employ multiple technologies that extend the capability of their own laboratories." The collaborations are all coming to fruition as the research is starting to pay off not only in terms of translating it into patient care, but also in terms of economic development and commercialisation opportunities, Dr. Casey added with pride.

Going forward, growth will be around partnerships as the school grows its research programmes in terms of collaborations. "We want to intertwine our activities with the research and academic activities in the SingHealth health system. To date, we have over 1,000 doctors who have faculty appointments with us and we are starting to cross appoint faculty and embed them within other institutions." This will continue to extend the reach and impact of Duke-NUS to bring about greater innovation and enhance the success in translational outcomes.

"These achievements could not have come about without the passion and innovative spirit of its researchers."
- Prof. Patrick Casey

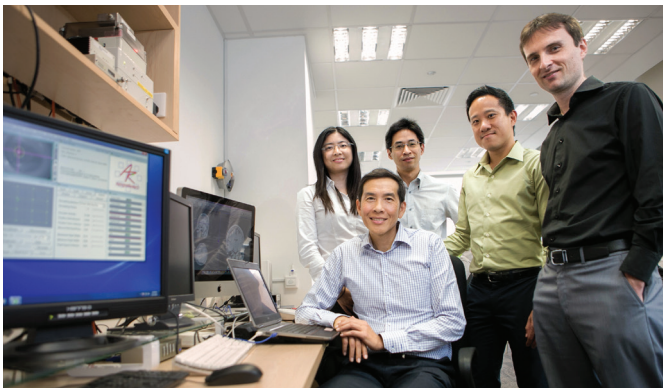
BRAIN IN FOCUS

Five faculty at Duke-NUS' Centre for Cognitive Neuroscience (CCN) are leading a brain revolution; they want to understand how the brain works and use this information to motivate people to make choices that result in better mental and physical health. The CCN team do this by augmenting their expertise while drawing on their colleagues' strengths in their respective fields.

"In a country like Singapore, with a predominantly East Asian population, hard work is paramount while adequate sleep is often neglected."
- Prof. Michael Chee

Their scientific interests and skill sets positively reinforce one another. Unlike researchers who work in much larger centres around the world, CCN researchers understand that collaboration is crucial for their relatively small and young programme to be competitive and stay relevant.

What does each of their teams do?



The CCN Team, (standing L-R) Asst. Prof. Helen Zhou, Asst. Prof. Brown Hsieh, Asst. Prof. Julian Lim, Asst. Prof. Joshua Gooley and Prof. Michael Chee (seated)

Prof. Michael Chee

Towards Healthier Sleep

Professor Michael Chee leads research that will ultimately improve people's health and more specifically, their choices regarding sleep. The Director of the CCN and Principal Investigator (PI) of the Cognitive Neuroscience Laboratory has spent the last decade and a half mapping how sleep deprivation affects brain and behaviour using both functional Magnetic Resonance Imaging (fMRI) and a variety of other tools. More recently, he has started evaluating the effects of sleep loss across the lifespan. An example of this thrust is a study in which his team intensively monitored 60 high school students for two weeks using behavioural tests, electroencephalogram (EEG) and brain imaging. The study is the first of its kind in the world, and will better define the impact of short sleep in teenagers - a group whose poor sleep habits could have serious untoward effects later in life. Happily, timely intervention could alter that course when habits are still in a formative stage.

At the other end of the lifespan, his team has also carefully followed up a cohort of older cognitively healthy Singaporean adults with brain imaging and behavioural tests for 10 years to characterise the trajectory of cognitive ageing in healthy Chinese adults. To observe is one thing but to intervene effectively is another. For example, his team has investigated the efficacy of EEG phase-locked acoustic stimulation delivered during naps, on memory.

"In a country like Singapore, with a predominantly East Asian population, hard work is paramount while adequate sleep is often neglected," said Dr. Chee, when explaining the relevance of his research in a local context. "Young people believe they are invincible but in reality, poor sleep eventually leads to loss of productivity and negative health consequences. Our goal is to design interventions relevant to improving sleep or diminishing negative impact of sleep loss appropriate for different stages in life."

Connecting the Dots

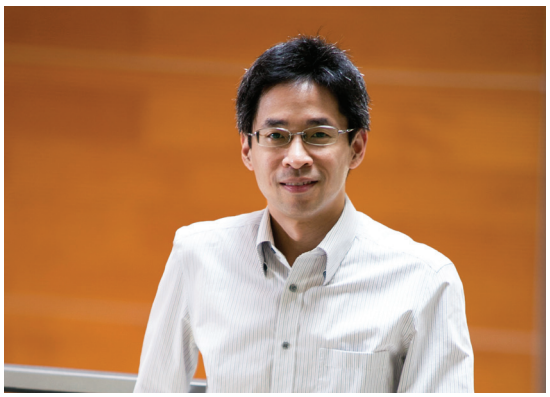
Assistant Professor Juan (Helen) Zhou's lab, the Multimodal Neuroimaging in Neuropsychiatric Disorders Laboratory, is focused on examining the structural and functional connectivity patterns of the brain, in other words, how different brain regions communicate with each other, in health and disease. This includes the link to ageing, neurodegenerative diseases, and schizophrenia. The team has identified several lines of evidence supporting network-based neurodegeneration, which is relevant and valuable in a rapidly-ageing society such as Singapore.

"I'm hopeful that our work on neuropsychiatric disorders could lead to deeper understanding of disease mechanisms and more accurate non-invasive biomarkers for early diagnosis and prognosis, disease progression tracking, and differential diagnosis."
- Asst. Prof. Helen Zhou

Asst. Prof. Helen Zhou

Currently her team is collaborating with researchers within Duke-NUS and throughout Singapore. Working on research related to brain structure and function underlying cognitive impairment and neural substrates associated with cognitive enhancement after interventions, Dr. Zhou and her team are passionate about translating brain imaging to tangible knowledge about patients and their disease.

"The developed neuroimaging assays could also act as objective monitoring tools for drug development and treatment design," shared Dr. Zhou.



Asst. Prof. Brown Hsieh

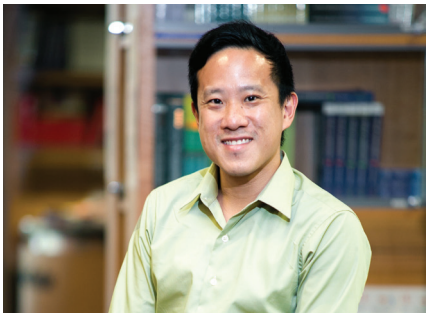
Making the Unconscious, Conscious

The research most difficult to describe comes out of the Brain & Consciousness Lab, helmed by Assistant Professor Po-Jang Hsieh or, Brown, as he is known at Duke-NUS. His team has been extending the research on the neural causes of consciousness. So far they have identified a few neural factors and brain regions involved in predicting conscious perceptions such as what we think of as unconscious or split second decisions.

"My research focuses on the neural correlates of consciousness, the causal relationship between neural activity and consciousness, and the functions of consciousness."
- Asst. Prof. Brown Hsieh

With the help of a recently awarded grant, Dr. Hsieh has now structured his work to investigate which brain regions are involved in higher-level decisions. Decision-making at elevated levels could be of interest to leaders, governments and the general public, as the study of how and why important decisions are made would provide us with an understanding of how it can be influenced.

"My research combines techniques from vision sciences, cognitive psychology, and cognitive neuroscience to investigate the cognitive and neural mechanisms that underlie human visual awareness," shared Dr. Hsieh.



Asst. Prof. Julian Lim

Making Sense Of Mental Fatigue

"Mindfulness training and meditation have been gaining prominence over the last decade... Down the road, our team is also planning to examine if this training has positive effects for those with symptoms of pre-dementia and mild cognitive impairment."
- Asst. Prof. Julian Lim

The newest addition to the Centre for Cognitive Neuroscience, Assistant Professor Julian Lim, is focused on the effects of mental fatigue on cognition and attention. An area of research that every working professional should be concerned about, Dr. Lim is looking into interventions and strategies that may mitigate the performance declines associated with mental fatigue.

Currently collaborating with Dr. Kinjal Doshi, a clinical psychologist from Singapore General Hospital, on a study on the effects of mindfulness training in a group of nurses. Dr. Lim is investigating whether the training affects quality of life, mental fatigue and changes in brain activity. The team also plans to study the interrelationships among these outcomes.

Dr. Lim shared, "Simple interventions that can have marked benefits for health and cognition are greatly relevant and in this case can have an immediate positive impact on nurses and their patients!"

Dr. Lim and his team are also working on using fMRI to study the effect of brief rest pauses during lengthy periods of monotonous work. A lot of research in the field has been focused on the correlates of performance decline, with relatively little attention paid to how individuals recover from fatigue. Previously unexplored, this research may have relevance for the design of work-rest schedules in industry and could help in the prevention of fatigue-related errors.

Sleep Matters

"I was fascinated by dreams, and actually looked forward to sleeping at night so that I could go through my dreams on the following morning."
- Asst. Prof. Joshua Gooley

Asst. Prof. Joshua Gooley

Assistant Professor Joshua Gooley is pretty clear about why he first got interested in the field of sleep research, "I slept a lot as a child, especially as a teenager," he confessed. The sleep expert now leads the Chronobiology and Sleep Laboratory at Duke-NUS where his team explores how sleep behaviour influences human performance. Recently, Dr. Gooley's team have examined how sleep deprivation impacts attention and vocabulary learning. They also conduct research on the pathways that modulate vigilance, sleep-wake cycles, and the sleep-promoting hormone melatonin.

Dr. Gooley shared that his team is currently working with ophthalmologists at the Singapore Eye Research Institute to develop a screening test to assess photoreceptor function. They have designed a short-duration protocol in which they measure how the pupils respond to different wavelengths and intensities of light, which gives information about the health of different types of retinal cells. This test may be used to detect glaucoma and other ocular diseases.

The team has already started testing in a few hundred patients, and initial results look promising. They are planning a larger study that will include patients with glaucoma and other eye diseases.

Tangible Outcomes

Drs. Chee, Zhou, Hsieh Lim and Gooley are working hard to educate people about the work that they do by consistently engaging with the media. Members of the team have appeared on television interviews, talked about their study findings with the press, and penned commentaries about their work and its relevance to society. They study humans, are well-steeped in neuroscience and are serious about translating their findings.

Other countries, other centres and other researchers have been developing their brand of neuroscience research for a long time. At the CCN, they hope to take findings out of the lab, to make significant international impact and to communicate the relevance of science to society, and beyond.

FOR THE LOVE OF SCIENCE: THE LONG AND REWARDING PHD JOURNEY

Milly flanked by Assoc. Prof. Ooi Eng Eong (left) and Prof. Duane Gubler (right)

Two Duke-NUS students who recently defended their PhD thesis, share the trials and rewards of their PhD journey, thesis defence, and the new and bright pathways ahead.

For Milly Choy, the culmination of having defended her thesis – the final examination that marks the end of her PhD journey – is much like the finale of a symphony, the satisfying sense of fulfilment that follows a crescendo of sound and activity. As for her peer, Nicodemus Oey, the thesis defence has been a humbling opportunity to present the work one has toiled on for four long years. The process of being able to offer something new to advance the field, he said, "is a necessary step to become a true discoverer of science."

"Finale of a symphony."
- PhD graduate, Milly Choy

For every PhD student, four to five years of work culminates in a public seminar in which the candidate provides evidence for his/her claim(s) in front of examiners, experts in their fields, and the public at large, who may question or refute these claims. This defence is the milestone that caps a myriad of other criteria: the completion of 25 credits of full-time coursework, a Qualifying Examination, the pursuit of getting these discoveries published in a peer-reviewed journal and the writing of a 200 to 400 page PhD dissertation. For each PhD candidate, it closes a chapter of their journey in medical science whilst opening another as they embark on a new path.

Unique PhD Experience

Milly, who graduated from Nanyang Technological University in 2010 with a BSc Hons in Biological Sciences, is part of the pioneer batch of the Duke-NUS PhD programme. Her work on the interaction of dengue virus with its hosts, the Aedes aegypti mosquito and humans, seeks to identify a potential antiviral drug. "My thesis investigates the role of a pathway that is critical for protein degradation in cells in the dengue virus life cycle," she explained. "We show that inhibition of this pathway, the ubiquitin proteasome pathway, is able to reduce dengue virus production in human cell lines and mosquitoes, as well as ameliorate signs of dengue in a wild type mouse model."

Working with luminaries in the field, Professor Duane Gubler and Associate Professor Ooi Eng Eong, she has benefitted greatly from their expertise. "Dr. Gubler has spent more than 50 years working on vector-borne diseases around the world, and his research has contributed greatly to our understanding of dengue," she pointed out. "His dedication to his work is something I strive to emulate." She also expressed gratitude for the mentorship she has received from all her professors. "The collective nature of the Emerging Infectious Diseases programme was a huge plus point for me, as all the professors were ever so willing to share their experiences and knowledge with PhD students," she said.

Looking back on her PhD experience, Milly, who will go on to work as a research fellow in Genome Institute of Singapore, A*STAR, reflected how

Nicodemus (centre), Milly (right) and their classmate

preparation and partnership with others has aided her in her work. "To me, the work starts from the first day you step into the lab," she said. "If you planned all your experiments well, and engage in frequent discussions with professors and fellow colleagues about your work, you should be able to write a good thesis. Having said that, a thorough understanding of what you are doing is essential for a successful defence!"

A Dream Made Reality

The eight-year long road to becoming an MD-PhD has been the fruition of a childhood ambition for Nicodemus Oey. Born in Padang, Indonesia, the young Nicodemus, who won a National Biology Scholarship to study in the University of Toronto, never had any doubt that he wanted to become a clinician scientist. This led him to join Duke-NUS. "Its vision of being an academic medical centre to train future clinician-scientists was a huge factor of my decision to apply," he said.

"A necessary step to become a true discoverer of science."
- Nicodemus Oey

His thesis on the molecular mechanisms involved in memory formation, is one he has spent four and a half years on, learning about a particular protein called PHF8 found in the nervous system. He ended up discovering a fundamental epigenetic 'switch' that turns genes on and off in response to neural activity. "If we are what we think, then my hope is that my work has contributed to understanding the very process by which we are able to do so," he explained. "This has implications in the discovery of novel treatments for extremely debilitating diseases such as Alzheimer's and Parkinson's, where patients' memories fail them."

It was a long journey towards the discovery, he shared. "In the beginning I was too busy trying to learn basic techniques, doing laboratory bench work, and just training to be a scientist. Over time as I grew more confident with my skills and ability to contribute results and insights, I started developing collaborations with prominent scientists and clinicians with a range of expertise." His mentors include Drs. Patrick Tan, Zhou Lei, Roger Beuerman, Helen Zhou, Ng Yee Sien and Sarah Lisanby. " They all have enriched my training immensely and have given meaning to the research I contribute to." In particular, he credits his achievements to his mentor, Associate Professor Antonius Van Dongen, an expert in molecular, cellular, and systems neurobiology. Nicodemus is grateful for the support

Nicodemus (left) with Ms. Hendrika M. A. Van Dongen (centre) and Assoc. Prof. Antonius Van Dongen (right)

and encouragement he received under Dr. Van Dongen's tutelage. "I can't remember how many times I have been stumped, at a total loss for how to make sense of the results that I see in front of me, but I do remember the numerous instances he has helped me through those tough times; every single time. I cannot thank Dr. Van Dongen and his wife, Margon enough for their unwavering support through these years, without which I highly doubt I could have even survived my first year as a budding scientist."

Describing his four years of medical school and four years of PhD work as a "long and arduous road full of dangers lurking in every corner," Nicodemus nevertheless said that it was all worth the slog. "Not one single drug has ever been approved without the years of hard work and dedication of researchers working well late into the night in laboratories. Not one single innovation has ever been made without the blood, sweat, and tears of the clinician or basic scientists putting their hearts and souls into what they do."

With the rise in dementia due to the rapidly ageing population, it is his hope of stopping what is a currently incurable, though highly debilitating disease, that drives him. "It is what makes me get up every morning and come back to the lab every day of the week." Already, his work in uncovering the mechanism that may alter the course of memory-impairing diseases has resulted in several direct applications. He has worked with Dr. Ng Yee Sien from Singapore General Hospital in a successful pilot clinical trial of a new combinational therapy for stroke rehabilitation. Dr. Sarah Lisanby, head of Duke University Hospital's Department of Psychiatry and Behavioral Sciences, has also expressed interest in developing new medications for treating memory impairment in depressed patients based on his work.

With his scientific journey far from over, Nicodemus reflects, "I remember being a first-year medical student in a young, new medical school, being asked to write a short sentence about my aspirations as a future doctor. I said: 'I aspire to contribute to making discoveries that benefit patient care, with Duke-NUS as the spearhead of advancement in basic and translational medical scientific progress.' I feel that I have been true to this goal, and hope to continue to keep this aspiration in mind as I go forward."

Photos by: Kenneth Goh

A TEXAN IN SINGAPORE

Dallasite (Texan) Dypti Lulla, a third-year M.D. student shares the value of senior-junior transmission of knowledge and TeamLEAD's "osmotic" abilities.

By Dypti Lulla

Medical school sure keeps you busy! I came to Singapore from Dallas, Texas, for a new adventure, a new perspective on health care and an opportunity to live close to my parents. It was a big change in environment when moving from a sprawling city like Dallas to a compact city like Singapore. I got new roommates, new classmates, and had some great new experiences. I toured the city and tried the local cuisine but mostly, I spent my time keeping an intense medical training schedule with few holidays. Now, more than two years have flown by in a blink of an eye and I have completed my sub-internship.

It feels like yesterday when I stepped into the wards for the first time as a second-year medical student and saw my seniors looking so professional and so calm amidst the chaos that typically characterises ward rounds. However, the tables have turned and now I have juniors from school who look to me for guidance and answers. As I have stepped into my seniors' shoes, I have discovered latent leadership abilities and it gives me great pleasure to help my junior colleagues, showing them around the wards and explaining approaches to various patient complaints. We have limited time before we graduate and I can attest to how quickly that goes by. Clinical medicine may seem overwhelming and demoralising, but it only gets easier with more practice so I always advise them to use their time wisely to learn and improve.

Year One for me was like jumping off a diving board into the deep end of a pool without knowing how to swim. There was a lot of study material to cope with and we were unsure if TeamLEAD would help us digest the vast amount of material. Despite being told repeatedly that it is the best study model, the sheer volume of the material makes you feel like you have learned nothing even after many hours of studying, reviewing, and memorising. Then, out of the thin air, the material seems to return to your brain and settle in when you are in the wards in Year Two. I consider it an educational miracle – or maybe it works by osmosis from all the times you end up falling asleep on your textbook!

Dypti (third from left) watches on as Swee Sen (second from right) tries his hand at intubation during the anesthesia clerkship at KK Hospital
(Photo credit: Dr. Wendy Teow)

With the material now in one's brain, all you have to do is organise the scattered pieces so that you have complete information available to you when it is needed. For example when a consultant asks you for the causes of fine crepitation on auscultation of lungs (the lungs sound like Velcro when you put your stethoscope to the patient's chest) – you may blurt out "idiopathic pulmonary fibrosis" (which essentially means no known cause of the lung condition), but not remember anything else which makes you sound unprepared, but may just be a case of bad categorisation.

"I have come to value the great leadership provided by the student leaders who step up despite their hectic schedules."
- Dypti Lulla

The hard work and long hours can make medical school very stressful, which is why I took up the role of Vice President of Welfare in the Student Council. It not only serves as an escape from endless hours of studying and worrying about classes, but also gives me a chance to organise events so we can get to know each other better outside the structured atmosphere of the classroom. Everyone needs a small break from time to time (and the occasional free food!).

The advantage of a small school is that you have the ability to form a net to support you when you are falling, not just as a student, but also as alums. My participation in the Student Council made me realise that the Duke-NUS community can come together to form a mosaic of diversity and excellence. I have come to value the great leadership provided by the student leaders who step up despite their hectic schedules. We have all dedicated our lives to serve others but amidst the constant stress of studying, exams, and rotations it is important to carve out time for rest and relaxation by going to the events for fun and games (and of course, those awesome ones organised by the Student Council!)

Student Council takes on a Perfect 10 challenge for the Annual Giving Campaign. Top (L-R) Anu, Dypti, Petty, Esther, Melissa, Liying and Aditi (bottom)

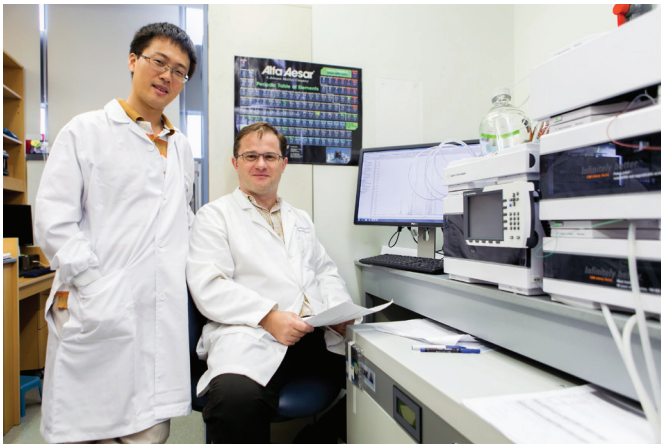
A PARTNERSHIP OF STRENGTHS

Two Duke-NUS researchers, Assistant Professors Sun Lei and Jean Paul Kovalik are gaining new insights into diabetes by combining science and clinical medicine. Dr. Sun, a PhD, delves into the basic science of how the development and function of fat, or adipose cells, impact the progress of diabetes. Dr. Kovalik, an endocrinologist, has research interests in energy burning pathways that drive the development of diabetes.

"We are studying how to harness brown fat in the human body so that it can be used to burn off excess blood glucose."
- Asst. Prof. Sun Lei

A Study of Brown Fat

Working together in Duke-NUS' Cardiovascular & Metabolic Disorders Programme, they have collaborated on several important studies and papers. One significant area of study for them is the relationship of human fat cells and diabetes.



Asst. Prof. Sun Lei (left) and Asst. Prof. Jean-Paul Kovalik (right) in their lab

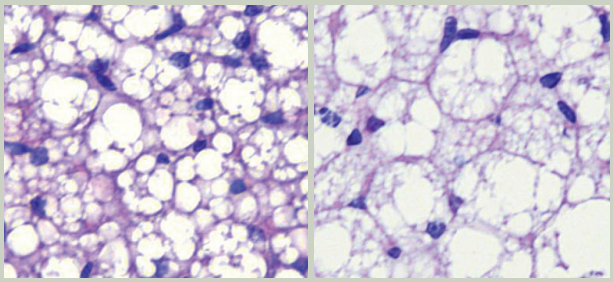
In a paper published in *Diabetes* in 2014, they explored the role of microRNAs in the regulation and maintenance of brown fat. This study may lead to new methods to activate this useful fat and develop new therapies for obesity.

"We are studying how to harness brown fat in the human body so that it can be used to burn off excess blood glucose," explained Dr. Sun. Brown fat burns fuel non-productively to make heat and its function – to keep them warm in cold weather – is well understood in animals. Dr. Kovalik went on to explain, "In humans, it was previously thought that only babies had brown fat which disappears as we reach adulthood. More recently, it has been discovered that adults too have small amounts of brown fat. This is of great interest in the diabetes world because if we are able to 'turn on' human brown fat, we can burn off excess calories and lose weight without the need for exercise." Activating a person's internal 'engine' to burn up excess calories can be a safe and effective way to control diabetes.

Bridging Science and Application

At present, Drs. Sun and Kovalik are working together with a pharmaceutical company, to determine how brown fat can be activated. This work underscores the benefits of finding synergy between basic science and clinical medicine to address important chronic diseases, they said. "By bringing together rigorous basic science and patient-derived knowledge, we can connect science with the delivery of treatments, and provide more tangible outcomes," said Dr. Kovalik.

Dr. Sun also pointed out the benefits of working with MD-PhDs such as Dr. Kovalik, "He acts as a translator and bridge between the science and clinical work, connecting us, the researchers, with doctors to further the bench-to- bedside transition." Facilitating such work are the various '-omics' facilities at Duke-NUS, including the Metabolomics Facility where Dr. Kovalik serves as Director.

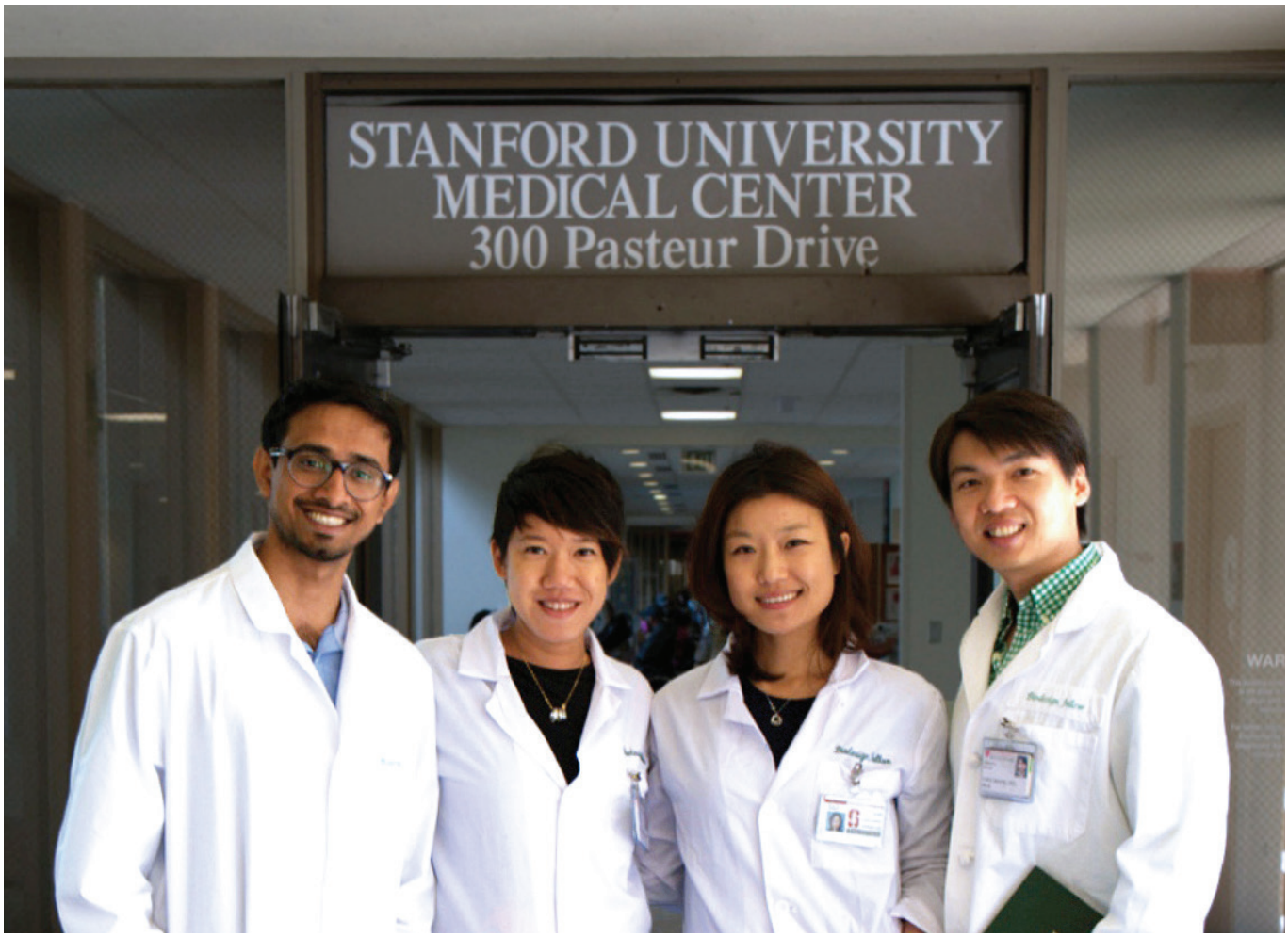


Micrographic images of brown fats

Brown fat samples

"Modern '-omics' has the potential to be used not only to predict the risk or severity of a disease, but fine-tune the therapy."
- Asst. Prof. Jean-Paul Kovalik

"We now have a suite of '-omics' tools at our fingertips: genomics looks at DNA changes, transcriptomics analyses RNA, proteomics looks at proteins and now metabolomics can be used to study biochemical pathways. Layering all these technologies together gets us information that was previously unobtainable, resulting in new insights," shared Dr. Kovalik. Samples obtained from doctors can be studied to identify the signatures of heart attacks, diabetes and kidney diseases even before they happen. "Modern '-omics' has the potential to be used not only to predict the risk or severity of a disease, but fine-tune the therapy. By analysing an individual's DNA, RNA, protein and biochemistry, treatment can be adjusted for more personalised approach to medicine."



Rena (second from left) with her Privi teammates (Photo credit: Rena Dharmawan)

A 'SURGEON-INNOVATOR' IN THE MAKING

Duke-NUS alumna, Dr. Rena Dharmawan, is part of a team that won $100,000 in start-up funding in NTUC Income's Future Starter competition. Rena, who was part of the inaugural batch of medical students at Duke-NUS, took a year off her residency last year to do a medical device innovation fellowship with Singapore-Stanford Biodesign (SSB). The engineer-trained surgical resident has always been interested in medical technology and medical devices. "I believe that with the right innovation, one can really impact the lives of millions of people. Bringing an invention from an idea to market and into the hands of patients is not easy, and thus I decided to take a year of my surgical training to do the SSB fellowship to really get my hands dirty, learn the biodesign process and build a network of mentors from Stanford and Silicon Valley. The fellowship has enabled us to identify solutions with market potential for unmet clinical needs and eventually commercialise them."

With her team, she worked on a medical device called *Privi* that aims to reduce bleeding and alleviate pain caused by haemorrhoids, which can be used at home. The disposable product tamponades the bleeding and soothes the pain from the haemorrhoids. *Privi,* which trumped 298 other teams to win the start-up competition, is now in prototype development and aims to begin clinical trials by the end of the year.

"The people that actually directly inspired my interest in this field are really the patients."
- Dr. Rena Dharmawan

It was during her surgical rotations during her second and fourth year that Rena first realised the challenge of treating haemorrhoids. "It is a difficult condition to treat and there is a huge treatment gap amongst the current home solutions to solve the symptoms of the disease. Although the disease is not life-threatening, it greatly affects the patient's quality of life and so I hoped to find better solutions to help this group of patients."

She credits the mentorship from her consultants in the colorectal department as well as her patients as her inspirations for the device. "The people that actually directly inspired my interest in this field are really the patients."

Looking forward to her return to hospital duties in April 2015, Rena hopes to further her twin interests in medicine and technology. "I hope to be a 'surgeon-innovator'; I want to continue practicing and to specialise in an area of surgery that is of my particular interest. This way, I can still keep up to date on the clinical front and ensure that any innovation we develop is relevant and will actually have an impact on patient outcomes."

Pursing a Passion, Finding Love and Family

Duke-NUS was more than a school for Drs. Rena Dharmawan and Daniel Yong. The aspiring doctors found more than their life's calling when they entered Duke-NUS in 2007. They found each other.

Over chemical equations, hours of study, debate and a dissected cadaver or two, Rena and Daniel met, fell in love, got married, and in 2014 welcomed their daughter, Noelle. Since then, balancing their medical careers, family life and Rena's recent fellowship has been challenging, but nonetheless rewarding for the both of them. Having their first child, particularly, has been "life-changing," said Rena.

"Our evenings and weekends now spent mainly hanging out with her and our in-laws. We have both decided that we will try our best not to take work home, so that we can give Noelle our full attention when we are back from work (especially on weekends)."

So while the avid travellers have had to forgo their annual goal of conquering at least two wonders-of-the-world (natural/man-made) for now, their own little wonder, Noelle, has more than made up for it. Daniel is a Senior Resident (Registrar) in the urology department at Tan Tock Seng Hospital and Rena will be returning to her residency at Singapore General Hospital after her fellowship ends.

Daniel and Rena's pre-wedding shoot at the old Duke-NUS campus

Daniel, Rena and baby Noelle

Daniel and Rena's graduation ceremony

Photos by: Rena Dharmawan

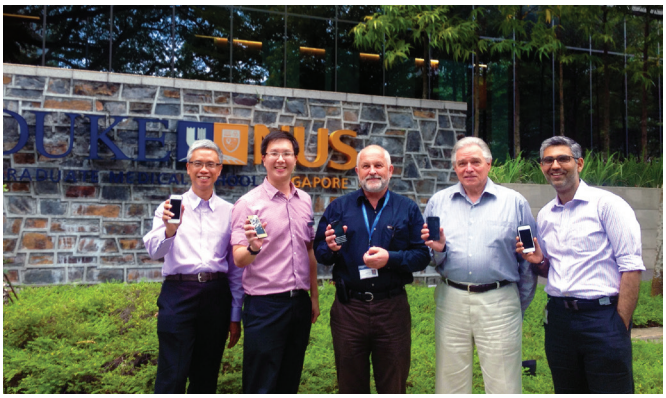
PARTNERSHIPS OF THE HEART

Speaker Prof. Howard Rockman from Duke University School, delivering his keynote presentation

Held in January this year, the Joint Duke/Duke-NUS Symposium, 'Synergizing Biomedical Research in Cardiovascular and Metabolic Disorders,' brought together leading researchers from Duke University, Duke-NUS and all over Singapore. The symposium featured experts presenting their research related to the clustering of metabolic syndrome, diabetes, hypertension, hyperlipidemia and cardiovascular disease. This is a global epidemic that is emerging as a major cause of mortality and human suffering in Asia. A major objective of the meeting was to develop productive partnerships and collaborations to enhance research in the field. The Symposium was the first activity to be held in 2015 by Duke-NUS to mark its 10th year.

The CVMD Symposium speakers

TESTING HEALTH APPS FOR REAL-LIFE



The iDAT Team: (L-R) Prof. Tan Ngiap Chuan, Glenn Goh, Prof. Truls Østbye, Asst. Prof. John Carson Allen and Assoc. Prof. Rahul Malhotra

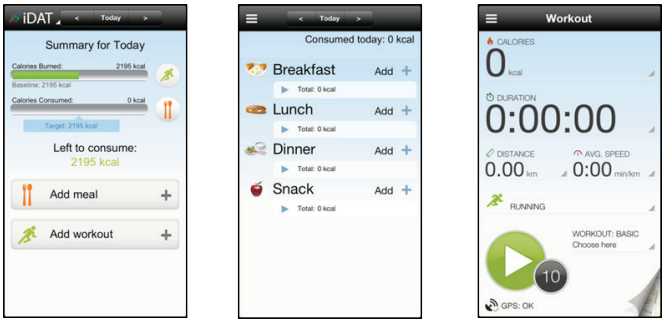
A recent study led by Duke-NUS fourth- year medical student, Glenn Goh, has provided insight into the usage pattern of mobile health applications or apps. The findings, published online in the top-ranked medical informatics publication, *Journal of Medical Internet Research*, give medical practitioners a useful framework for evaluating future health app use for patients.

Self-management plays an important role in maintaining good control of diabetes and mobile phone interventions have been shown to improve self-management. While many doctors recommend mobile health apps to patients to better manage chronic conditions, it is not known which patient groups to target and who are more likely to actually use the apps.

Addressing this gap, Glenn worked with his mentors Professor Tan Ngiap Chuan (SingHealth Polyclinics); Assistant Professor Rahul Malhotra and Professor Truls Østbye (Duke-NUS Health Services and Systems Research Programme); Assistant Professor John Allen (Office of Clinical Sciences and Centre for Quantitative Medicine) and Sylvaine Barbier to test the usage pattern of the caloric-monitoring mobile health app, iDAT. iDAT is an "interactive Diet and Activity Tracker" devised by collaborators and the Health Promotion Board of Singapore.

The study involved 84 patients with type 2 diabetes mellitus from a SingHealth polyclinic, who were instructed to use the iDAT app to record food intake and exercise frequency for a period of eight weeks. Results showed that only about two in 10 patients used the application consistently over the eight week period. These consistent users tended to be females and individuals who at baseline were motivated to improve their exercise frequency.

"Our study gives doctors a better idea of patients' app usage when introducing health apps to patients to help manage their chronic conditions," explained senior author Dr. Østbye. "Previous mobile phone interventions usually provide regular reminders or incentives for patients to use the apps. Ours did not, which renders more realistic results that are based mainly on patient self-motivation."



The "interactive Diet and Activity Tracker" (iDat) app helps patients to monitor their food intake and exercise frequency.

Photos by: Glenn Goh

DETECTING HIGH-RISK HEART PATIENTS WITH 'TITIN'

Prof. Stuart Cook

Tanoto Foundation Professor Stuart Cook, Deputy Director of the Cardiovascular and Metabolic Disorders Programme at Duke-NUS, led a study that identified genetic mutations that cause dilated cardiomyopathy (DCM). DCM is a common heart condition that affects one in 250 people and can lead to progressive cardiac failure, irregular heartbeats and sudden death.

Published in *Science Translational Medicine*, the research sequenced the gene that encodes the muscle protein called titin in 5,267 people. Titin gene mutations have previously been associated with DCM, but many people also have variations that are benign.

The new findings from this massive genetic sequencing will pave the way for more accurate diagnosis. This is because now, Dr. Cook's team have been able to distinguish between harmful and harmless mutations because they can pinpoint exactly where the mutations that cause DCM occur. Doctors can now use this information to screen high-risk patients and thus take a more proactive step in addressing the disease.

"We can use this information as a genetic blueprint to screen patients' families and identify those at risk of developing the disease and also help them to manage their condition early," explained Dr. Cook, who is a senior consultant at the National Heart Centre Singapore (NHCS).

STaR Awardee Dr. Cook also commented on why this recent study was ground-breaking. "This would not have happened five years ago - the technology we have now, combined with the expertise in NHCS and Imperial College London made this breakthrough possible."

The research was funded by the Medical Research Council (MRC), the British Heart Foundation, the Fondation Leducq, the Wellcome Trust, the National Institute for Health Research (NIHR) Royal Brompton Cardiovascular Biomedical Research Unit and the NIHR Imperial Biomedical Research Centre.

Dr. Cook, who is also Director of National Heart Research Institute Singapore, plans to extend this research to Singapore as previous titin research has mainly screened Caucasian patients. He hopes to confirm if the mutations are the same for Asian patients, which will help doctors in the region tailor their respective diagnosis and treatment.

The two-year local study on the link between titin gene truncations and dilated cardiomyopathy is supported by a research grant from the Goh Foundation and the National Medical Research Council. Dr. Cook's team of collaborators are currently in the process of recruiting participants. They hope to screen between 700 to thousands of patients in order to compile the most comprehensive database on healthy and non-healthy participants.

POTENT DENGUE NEUTRALISING ANTIBODY FOUND

Assoc. Prof. Lok Sheemei

A study led by Associate Professor Shee Mei Lok and Research Fellow Guntur Fibriansah has identified a super-potent antibody which is only required in minute amounts to neutralise the dengue virus. Published in the journal *Nature Communications,* their work showed how a newly identified antibody, 5J7, is highly effective in killing dengue virus. Only 10-9 g of the antibody is needed to stop the infection of dengue serotype 3 virus (DENV-3).

The researchers, from the Emerging Infectious Disease Programme at Duke-NUS, isolated 5J7 from 200 different candidate antibody molecules by studying blood samples from a dengue infected patient. They showed that each 'arm' of the antibody is effective in grabbing three surface proteins on the surface of the virus at the same time. In addition, the sites on the virus where the antibody bound to were critical for the virus to invade cells.

"This kind of binding with the virus has never been observed and it explains why the antibody itself is so highly potent," explained Dr. Lok.

The dengue virus is estimated to be endemic in 100 countries and is a huge burden on healthcare systems. Till now, there is no licensed dengue vaccine or therapeutic agent because the presence of four circulating virus serotypes (DENV1-4) complicates the development of a cure. This new finding gives hope for the development of effective dengue treatments.

Dr. Lok's lab has already discovered antibodies that are effective against DENV-1. Her strategy to develop a safe therapeutic is to combine four antibodies that each bind and potently inhibit infection of each of the dengue virus serotypes.

"We need to test the efficacy in mouse models first and then move to clinical trials," said Dr. Lok about the next step after this promising finding. "We are optimistic that we will make a treatment breakthrough within these few years but antibodies against all the other serotypes have to be identified first."

This study is a collaboration between researchers from Duke-NUS, the University of North Carolina and Vanderbilt University. It is supported by the National Research Foundation Singapore under its Research Fellowship Scheme (NRF RF Award No.: NRF-RF2009-01) and the Singapore Ministry of Education Academic Research Fund Tier 3 grant. (MOE2012-T3-1-008).

SEARCHING FOR DENGUE'S ACHILLES HEEL

Prof. Subhash Vasudevan (left) and Dr. Moon Tay (right)

Professor Subhash Vasudevan together with Dr. Moon Tay, a recent graduate of the Integrated Biology and Medicine (IBM) PhD programme at Duke-NUS have made progress in understanding the interactions of two proteins that are key in dengue virus (DENV) replication. This work, which was published in the *Journal of Biological Chemistry*, gives researchers a potential target on which to focus dengue therapeutics.

"Drug discovery research happens in a defined sequence and target finding/validation is a very important first step in the process. The search for 'direct-acting antiviral drugs' by targeting the so-called 'low hanging fruit' - the essential enzymatic activities catalysed by the viral proteins - is proving to be a tough nut to crack for DENV," said Dr. Vasudevan from the Emerging Infectious Diseases Programme at Duke-NUS. "So we try and find targets for dengue therapeutics at the viral RNA and viral protein interaction level as such interaction drives viral RNA replication in DENV infected cells."

Among the non-structural (NS) viral proteins, NS3 and NS5 contain the enzymatic activities that are crucial for viral RNA replication. Dr. Tay, as part of her PhD studies, used biochemical, biophysical and reverse genetics approaches to discover an important Achilles heel in the essential interaction between DENV NS3 and NS5 proteins: NS3 residue Asn-570 is required for interaction with NS5. Introduction of the mutation into a DENV2 infectious cDNA clone revealed that virus replication is considerably attenuated and that NS3-NS5 interaction has an important role in the balanced synthesis of plus- and minus-strand RNA for robust viral replication.

"The molecular details of the interaction site give researchers a viable target site when designing antiviral drugs," added Dr. Tay, a pioneering member of the IBM PhD programme's first cohort. "In addition, the ability of the NS3 mutant virus to synthesise low level of viral RNA and viral protein makes it a potentially interesting dengue vaccine candidate."

Study authors include collaborators from Duke-NUS, the Lee Kong Chian School of Medicine and the School of Biological Sciences at Nanyang Technological University. Funding for the research was provided by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme (NMRC/TCR/005-GMS/2008) administered by the Singapore Ministry of Health's National Medical Research Council, the Singapore Ministry of Education Academic Research Fund Tier 3 grant (MOE2012-T3-1-008) and the Duke-NUS Signature Research Programme, with funding from the Ministry of Health.

STRATEGIES FOR NEW FLU VACCINE

Asst. Prof. Vijaykrishna Dhanasekaran (left) and Assoc. Prof. Gavin Smith (right)

A study, led by Assistant Professor Vijay Dhanasekaran and Associate Professor Gavin Smith from Duke-NUS, could help make flu immunisation programmes more effective; by better targeting vaccines or by eventually eliminating one of the flu lineages completely.

Four influenza virus lineages circulate in humans to cause three to five million cases of illness and 250,000 to 500,000 deaths yearly. However, most studies have focused on influenza A as they are believed to be more common in humans and because they have periodically emerged from animals (e.g. bird flu or swine flu) to cause human pandemics.

Influenza B viruses, on the other hand, have continuously circulated among humans since their first detection in 1940 and diverged into two lineages, the Victoria and Yamagata. Vijaykrishna et al have undertaken the largest comparative analysis of human influenza B viruses to date.

This study reveals that a focus on influenza B could be more strategic. "Our research shows that school-aged children are more susceptible than adults to influenza B virus lineages, especially the Victoria lineage," explained first author, Dr. Dhanasekaran from the Emerging Infectious Diseases Programme at Duke-NUS.

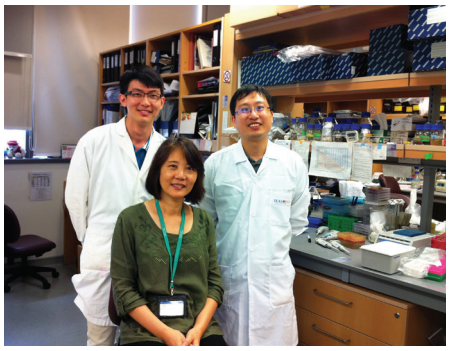
This indicates that it may be useful to give children the newer – though more expensive and difficult to prepare – quadrivalent influenza vaccines that target all four lineages, instead of the more commonly administered influenza vaccines that target both influenza A lineage viruses but only one influenza B lineage virus.

Also significant: the discovery that influenza B Yamagata viruses evolve much more slowly than influenza B Victoria viruses. This could mean that a wide-scale quadrivalent influenza vaccination could eradicate the slower Yamagata lineage from humans.

The study was authored by scientists from Australia, New Zealand, the United States, Switzerland and Singapore and marked a major collaboration between Duke-NUS and the Bioinformatics Institute (BII), Agency for Science, Technology and Research (A*STAR).

Published in the journal *eLife*, the study was supported by grants from the US National Institutes of Health, the Australian Government Department of Health and Ageing, the Swiss National Science Foundation, the Australian National Health and Medical Research Council and A*STAR joint grant (12/1/06/24/5793), the Singapore Ministry of Health's National Medical Research Council under its Individual Research Grant (NMRC/GMS/1251/2010), the Singapore Ministry of Education Academic Research Fund Tier 2 grant (MOE2011-T2-2-049) and the Duke-NUS Signature Research Programme, with funding from the Singapore Ministry of Health and A*STAR.

UNDERSTANDING AUTOPHAGY IN CANCER: THE COMPLEX ROLES OF FoXO TRANSCRIPTION FACTOR



The authors of the study (L-R): Zhu Wanlong, Asst. Prof. Mei Wang-Casey and Teh Jing Tsong

Autophagy, or "self-eating," as it is translated from Greek, has garnered a lot of attention in the field of cell biology. It appears that eukaryotic cells have evolved a way to survive the condition of nutrient deprivation and sustain vital cellular functions by consuming the non-essential part of themselves.

This amazing machinery is well conserved in many organisms, from baking yeast to man, which supports its fundamental importance. In fact, the disruption of autophagy leads to multiple pathological conditions, such as cancer and neurodegeneration. The level of autophagy relies on a delicate balance; too much or too little autophagy has proved detrimental to cells. It is therefore fundamentally important to understand the regulation of pro-autophagic and anti-autophagic process, specifically in the context of health and disease.

A recent study, by PhD students Zhu Wanlong, Tong Honglian, and Teh Jing Tsong in Assistant Professor Mei Wang's laboratory (Duke-NUS Cancer and Stem Cell Biology Programme), focusing on FoxO proteins, has shed new light on the regulation of autophagy. FoxO proteins are well investigated autophagy regulators. Previously, it was generally acknowledged that FoxO1 and FoxO3a stimulate autophagy, through their function in the nucleus as transcription factors. However, almost all studies have been done in non-cancerous cells. This new Duke-NUS led study investigated whether the FoxO proteins function similarly in cancer cells to promote autophagy. This research explores the new and complex functions of these important regulators, which may provide new opportunities for cancer therapy.

Dr. Wang's team made several discoveries in the recently published paper. They showed that it is as a cytosolic, not nuclear protein, where FoxO1 works as a master coordinator in metabolism to positively regulate autophagy. Contrary to past studies, the work demonstrates that FoxO3a can also serve as a negative regulator of autophagy in some cancer cells, and it does so by suppressing the level of FoxO1. This revealed a previously unrecognised way that the sister proteins interact, and that the regulation of autophagy by FoxO1 / FoxO3a is not solely performed through the commonly recognised conduit of mTOR signaling. In addition, the study highlights the likelihood that FoxO3a regulation of autophagy is different in cancer cells compared to normal cells.

A major challenge in cancer therapy is to differentially kill cancerous cells while sparing the normal cells. Therefore, identifying the differences in regulation by FoxO3a between benign and cancer cells is significant. "As treatment usually involves inactivating a cancer promoting protein, the fact that suppression of the function of FoxO3a induces autophagy and inhibits cell proliferation, presents therapeutic opportunities," explained Dr. Wang and her colleagues.

This work was published in the journal *PLOS ONE,* and was supported by funding from the Duke-NUS Signature Research Programme, with funding from the Singapore Ministry of Health.

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