



## Highlights

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### Message From The Dean

Welcome to the first issue of Vital Science for 2013. I hope your holidays have been filled with good cheer.

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- PM Lee Visits Duke-NUS
- New Institute for Research Launched
- Recognizing Research Excellence
- Fostering the Spirit of Giving



### Understanding Choices at the End-of-Life

What choices do people make at the end-of-life and how can we understand these so as to provide the right services, comfort, dignity and support at this inevitable part of life?

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### Learning From Ezzy, a Cancer Patient

The process of learning medicine is not just from books and doctors, but from the patients we meet as well.

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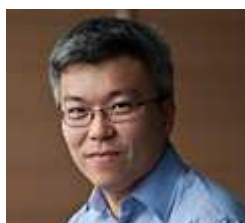
## Reflections of a First-Year MD/PhD Student

When I first started my undergraduate studies in Pharmacology at University College London (UCL), the idea of postgraduate studies was a faraway thought.

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PM Lee Visits Duke-NUS  
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## Life After Duke-NUS

It has been more than a year since I graduated from Duke-NUS. For the past year, I was in the transition year residency program, putting in long hours and surmounting the many potentially traumatic calls.

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## VITAL SCIENCE

This e-communications update is produced by the Office of Communications and Development  
Editorial team: Janice Tan, Wee Lai Ming (Duke-NUS) and Sheralyn Tay

*Our banner story: Message From The Dean. Read the story [here](#).*

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## Message from the Dean



*Dean Ranga Krishnan (second from left) shares a light-hearted moment with alumni from the M.D. Class of 2011. From left: Dr. Karen Nadua, Dr. Lim Kheng Choon and Dr. Ong Liming*

Welcome to the first issue of *Vital Science* for 2013. I hope your holidays have been filled with good cheer.

2012 was a great year for the school. It has been a year of growth as our efforts over the past seven years have gained traction and brought us further recognition. I want to thank our internal and external stakeholders, and our partners, for your contributions that have made 2012 a success. I'd like to share with you my thoughts on what I feel are some of the more notable developments.

Just looking at the numbers alone, we have done well over the past seven years. Our researchers have published over 700 journal articles, filed 46 invention disclosures and 31 patent applications, for which three licenses were awarded. They have also garnered over S\$156 million competitive research dollars and over 30 competitive research scientist awards. Two clinician-scientists, Professor Karl Tryggvason and Professor Stuart Cook, who are world-renowned for their work in cardiovascular and metabolic diseases, have joined us. They each received significant research grants through the Singapore Translational Research Investigator (STaR) Awards and would develop key programs in cardiac disease and diabetes. Professor Linfa Wang has also joined the school and will lead the Emerging Infectious Diseases program to even greater heights.

On the education side, TeamLEAD, Duke-NUS' signature pedagogical approach, has been recognized by the Association of American Medical Colleges (AAMC) as a major breakthrough in the teaching of medicine. Equally important, our TeamLEAD approach has gone beyond medical

teaching to other areas of learning at Duke University in the US and elsewhere. This is also significant for Duke-NUS as it is our way of giving back to Duke and to evolve and enhance the way they teach. This is a concrete example of our contribution to education that has far-reaching impact beyond Singapore.

Our research-intensive training for medical students has worked well – our students have built a portfolio of 86 published research papers in the three years that they have been engaged in research.

## **A strong Academic Medicine culture**

Duke-NUS has launched two important institutes to deepen our education and research thrusts with SingHealth.

The Academic Medicine Education Institute (AM•EI) will push new boundaries in learning to transform the practice of health care education in all areas, from medicine to nursing, allied healthcare professions and more. This will help to nurture and train future generations of healthcare professionals and thus raise the quality of patient care in the long term.

Meanwhile, the Academic Medicine Research Institute (AMRI) provides a research career-enabling infrastructure to develop clinical investigators, research clinicians and scientists. AMRI interfaces with SingHealth's nine Academic Clinical Programs (ACPs) established (as at Nov 2012). By boosting the culture of research excellence, AMRI adds the required resources to our pursuit of translating research to improve healthcare. Already, a number of significant research discoveries are being translated to drive improvement in patient care.

I am also pleased that our school has coalesced and enhanced our five signature research programs in 2012 and connected our research to the clinics.

Last year, we saw our bench-to-bedside efforts become a reality for a number of important studies. From the discovery that Asians have a specific gene deletion that decreases the effectiveness of certain cancer drugs, to the strides made in gastric cancer using our genomics platform, to uncovering new trends in emerging infectious diseases research, to running a clinical trial to test an antiviral drug, Celgosivir, as a treatment for dengue fever, these studies are making great impact and in an unusually short span of time. In medicine, where it takes years to bring studies to human trials, the speed at which we have managed to engage in translational medicine is truly significant, thanks in part to you our faculty, and to our collaborations and bridges with clinical partners like SingHealth and other institutions.

## **Prime Minister Lee visits Duke-NUS**

In a strong show of support by Singapore stakeholders to Duke-NUS, Singapore's Prime Minister Lee Hsien Loong, paid a visit to the school on December 6. He was accompanied by the Minister of Health Gan Kim Yong, Minister of Education Heng Swee Keat, and Second Minister for Home Affairs and Minister of Trade and Industry S. Iswaran.

PM Lee was briefed on key Duke-NUS highlights that included our impactful innovations in medicine, education and research that are transforming the shape of healthcare in Singapore. It was also a chance to demonstrate the synergy Duke-NUS has, with its academic partner, SingHealth, in our integrated and coordinated education and research approaches.

Read more about PM Lee's visit [here](#)

## Valuable leadership: old and new



Mr. Tony Chew



Mr. Kai Nargolwala

The foundation of many of these successes has stemmed from the efforts of Mr. Tony Chew, who chaired the Duke-NUS Governing Board from its inception in 2005 to 2012. Mr. Chew has in the last seven years given an incredible level of support and hard work to connect, facilitate, interact with, and represent us to our various stakeholders so that we have been able to find a good fit in Singapore, and to build ties and mutual understanding with our various partners.

His hard work has played a key role in helping us to flourish here, understand the Singapore context and structures and anticipate challenges. We are thankful for Mr. Chew's efforts and are indebted to him for bringing Duke-NUS to where it is today. Taking over Mr. Chew's chair in 2013, we welcome Mr. Kai Nargolwala, whose wide experience in the financial world will help bring added dimension and new perspectives to our growth.

## Going forward

This new year not only brings a new chairman – but a renewed focus for our school. 2012 has been a year of establishing a new partnership in Academic Medicine with SingHealth; and 2013 is a year of consolidation as we work synergistically to deepen this partnership in both education and research. Not only do we hope to further medical education across various disciplines with the AM•EI, we also hope to nurture more clinically-oriented researchers with the AMRI. Our hope is to leverage on our mutual strengths by integrating SingHealth's clinical specialities with our strong research and education prowess to transform healthcare and bring more medical discoveries closer to patients. Apart from this, we aim to build new initiatives and innovations in medical technology to improve healthcare.

These are indeed exciting prospects. I thank you for your continued interest in Duke-NUS and our journey. If you have been reading our *Vital Science* e-newsletter regularly, we will continue to leverage on this platform to bring you news of developments in academic medicine, education and research in each issue. The newsletter is also available in a print-friendly format and in print (by request only).

Best wishes for 2013 and may this be a year of fulfilment for you and your family.

## Dean Ranga Krishnan

*Note: Information as at 6 December 2012*

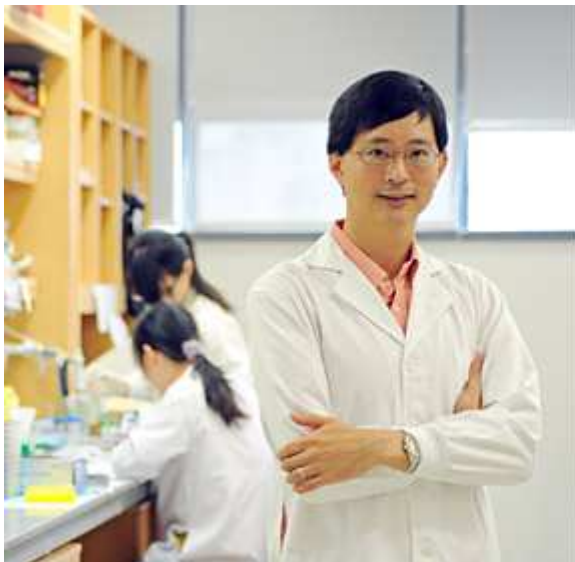
More: [Achievements at a Glance \(Education and Research\)](#)

## Research Highlights (2012) and Outlook for 2013

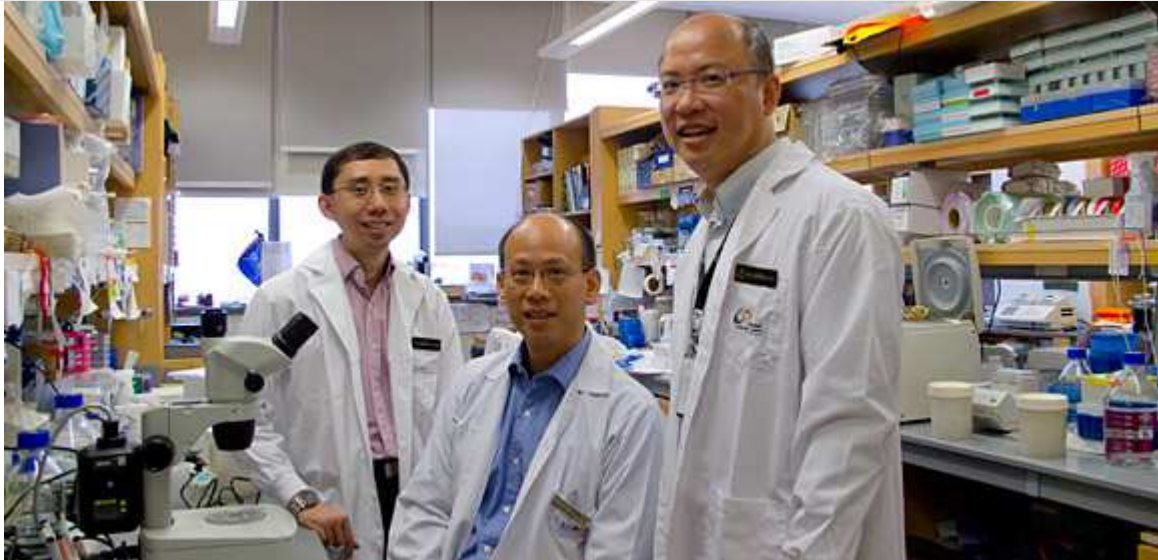


“ 2012 has been a great year for Duke-NUS research. We are producing leaders of change and innovation, and are developing a strong culture of collaboration. Our success rests on these accomplishments, which in turn improves the practice of medicine and brings crucial resources to the school. ”

Prof Patrick Casey, Senior Vice Dean for Research (left) with Prof Shirish Shenolikar and Prof Thomas Coffman



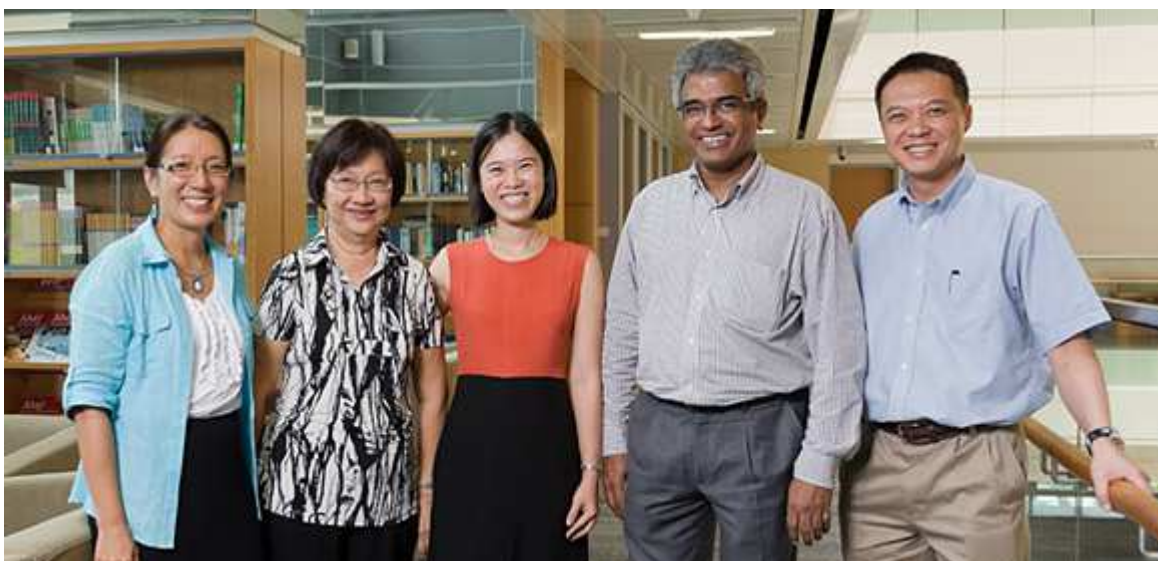
Research Discoveries | Bile Duct Cancer: Prof. Patrick Tan (left), Prof. Teh Bin Tean and Assoc. Prof. Steve Rozen (in blue shirt) led an international study which identified genes that are mutated in bile duct cancer. This discovery greatly increased our understanding of how bile duct cancer develops and it also paved the way for finding more appropriate and effective treatment against this malignant cancer with a particular prevalence in Southeast Asia. These same investigators also identified numerous new subtypes of gastric cancer that are triggered by environmental factors. These discoveries pave the way for better understanding and treatment of the killer disease.



Research Discoveries | Cancer Drug Resistance in Asians: Assoc. Prof. Ong Sin Tiong (seated) discovered a gene variant that explains why certain highly successful cancer drugs do not work on some people of East Asian descent. Discovering how the gene variant caused the resistance also allowed the researchers to overcome this drug resistance with a new class of drugs under development. The researchers are also working with the commercialisation arm of A\*STAR to develop a rapid diagnostic test for the gene variant. Collaborators in photo (left & right): Dr Charles Chuah (SGH) and Dr Darren Lim (NCCS).



Research Discoveries | Genetic Basis of Autism: Dr. Steve Rozen and colleagues sequenced the exomes of a series of genes and found gene mutations that affect brain development. This exciting development can lead to better diagnostics and treatments for autism.

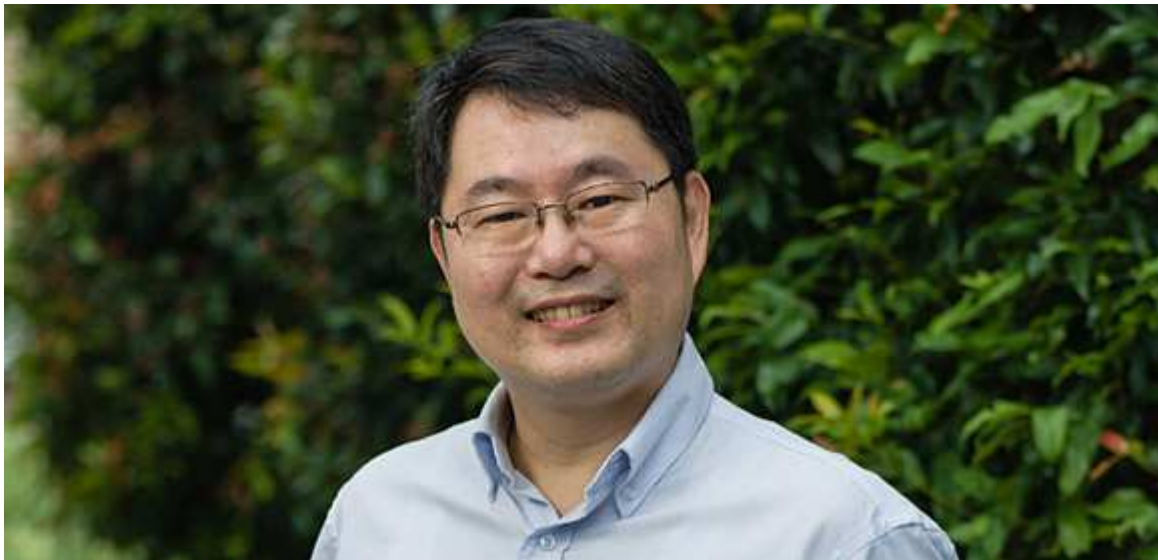


Medical Treatment | Dengue: The first trial of a new antiviral drug is being carried out in Singapore based on the insights of Assoc. Prof. Subhash Vasudevan from the EID Program. This is the first clinical trial emanating directly from discovery at Duke-NUS involving the antiviral drug, Celgosivir, to determine whether the drug can be used as a treatment for dengue fever. This proof-of-concept trial is part of the STOP Dengue Translational Clinical Research Program. Photo (L-R): Dr Cynthia Sung,

Mrs Catherine Chua, Dr Jenny Low (SGH), Dr Subhash Vasudevan and Dr Ooi Eng Eong.



Medical Treatment | Vaccine for Dengue: Asst. Prof. Lok Sheemei, Assoc. Prof. Ooi Eng Eong (2nd and 3rd from left) and Adjunct Prof. Shi Pei Yong from the EID Program collaborated with a team of NUS scientists to identify and characterize a specific human antibody against dengue virus serotype 1. This antibody can potentially be used as a therapeutic or preventive agent for dengue virus infection.



Medical Treatment | Fatty Liver: Assoc. Prof. Paul Yen demonstrated how thyroid hormone increases oxidative metabolism. This novel mechanism is important for maintaining lipid homeostasis within the liver and suggests that it may be a novel target for drug therapy for non-alcoholic fatty liver disease, an epidemic condition for which there is no proven drug treatment currently.



Medical Treatment | Brain Computer Interface as a Treatment for ADHD: This joint project by Assoc. Prof. Lee Tih-Shih with A\*STAR and IMH has shown that use of this device improves attention in children with attention deficit disorder. The technology



has been licensed to Atentiv.



Health and Health Policy | Negative Effects of Sleep Deprivation: Prof. Michael Chee, one of Singapore's first STaR awardees, has published a series of studies showing that sleep deprivation increases one's propensity for distraction and sensitivity to positive rewards, while diminishing sensitivity to negative consequences. These findings have direct relevance to areas such as security services and problem gambling as sleep deprivation makes gambling even more tempting for many people.

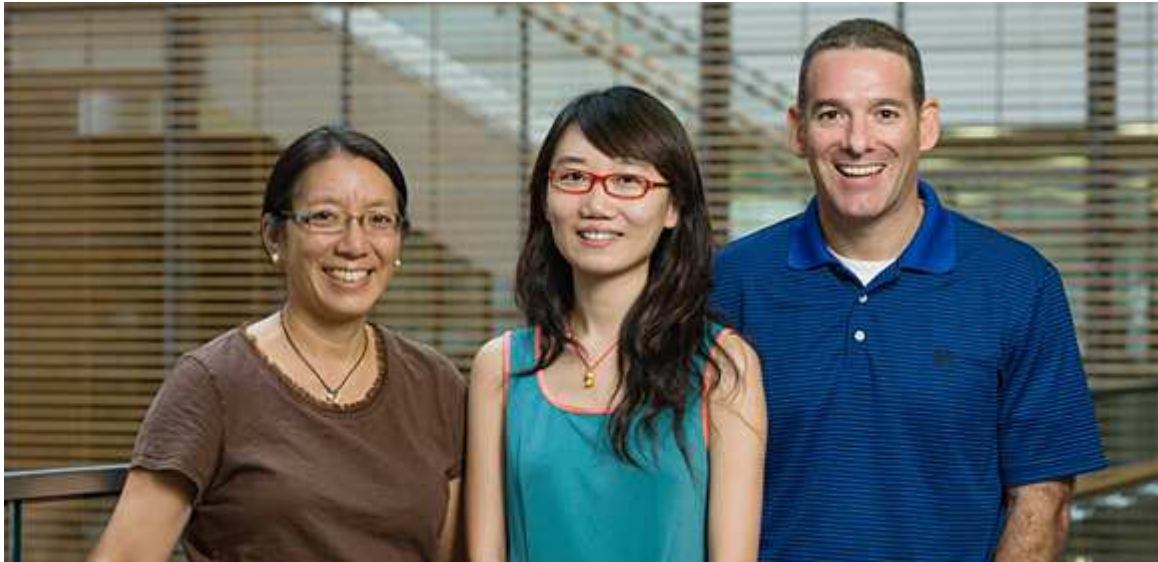


Health and Health Policy | Perspectives on End-of-Life Care in Singapore by the Lien Centre for Palliative Care revealed that Singaporeans value pain-free end-of-life care and prefer to pass away at home rather than have an extra year of life. These findings have implications on the focus of government subsidies and policies.



Health and Health Policy | Model for Assessing Medical Tests: Prof. David Matchar from the HSSR Program, also a STaR awardee, led a group of researchers from the USA to develop a methods guide for the optimal conduct of systematic reviews of medical tests. This comprehensive guide provides an efficient model for systematic evaluation of medical tests and promotes

the importance of establishing links between medical tests and patient health improvement before the commencement of any study.



Health and Health Policy | Test for screening for drug toxicity: Asians who carry the HLA-B\*1502 allele have an elevated risk of developing Stevens-Johnson syndrome and toxic epidermal necrolysis when treated with certain anti-epileptic drugs. The study showed that it is more cost effective to perform genetic testing on Chinese and Malay patients in Singapore before prescribing carbamazepine (an affordable but potentially hazardous anti-epileptic drug) to prevent serious adverse drug-induced reactions. Due to the prevalence of the risk allele in Asian population, this finding will be highly relevant to patients in other Southeast Asian countries such as Malaysia, Thailand and the Philippines. [Photo: Dr Cynthia Sung, Ms Dong Di and Dr Eric Finkelstein]



Professor Patrick Casey Senior Vice Dean (Research)

“ Our goal for 2013 is to continue to strengthen the school's competitiveness in research, which includes enhancing our ability to obtain and effectively deploy support from all sectors – public, private and commercial. A key element of our success is partnerships that we have developed with entities across Singapore and indeed throughout the globe. These strategies will help us realize our vision as one of the world's premier research-intensive medical schools ”

- Professor Patrick Casey, Senior Vice Dean (Research)

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## Understanding Choices at the End of Life

What choices do people make at the end-of-life and how can we understand these so as to provide the right services, comfort, dignity and support at this inevitable part of life? The critical need to tackle these complex issues has taken on a sharper focus in recent years given Singapore's ageing population.

Speaking on plans for the coming year, newly appointed Director of the Lien Centre for Palliative Care (LCPC) Dr. Eric Finkelstein told *Vital Science* that he and his team of researchers intend to intensify research focused on ensuring that individuals receive end-of-life care consistent with their preferences. "We also aim to increase collaborations with entities in Singapore that provide palliative care services such as the Department of Palliative Medicine (DPM) at the National Cancer Centre (NCC) and the members of Singapore Hospice Council, among others. Another area of focus is to work on the issues identified in the National Strategy for Palliative Care, a report coordinated by LCPC under commission from the Ministry of Health. This report provides a framework for future research and education."

Dr. Finkelstein – whose research focuses on understanding the economic causes and consequences of health behaviors and choices that underpin those behaviors – also hopes to drive increased understanding of end-of-life choices so as to better inform policymaking and service provision. "The aim is to understand what people want at the end of life so we can ensure those wants can be met at a reasonable cost," he explained. For example, if Singaporeans prefer to spend their final days at home, we need to identify appropriate models of care that make that possible on a systematic basis.

### The choices at end of life

One study led by Dr. Chetna Malhotra of LCPC, with input from Dr. Finkelstein and other colleagues in the Duke-NUS Health Services and Systems Research program and NCC DPM, focused on quantifying end-of-life care preferences of Singaporeans aged over 50 using a national survey. The community-based survey of over 500 participants revealed that moderately life-extending care was of relatively low value. In fact, participants placed a significantly higher value on pain management than on extending the period that the individual lives with a terminal illness, even if it increases survival by one year or more."



*Dr. Eric Finkelstein, Director, Lien Centre for Palliative Care.*

These findings are relevant because individuals may make decisions on health insurance and advance care planning when they are healthy, based on what they believe they would want when they fall ill,” said Dr. Finkelstein.

However, Dr. Finkelstein noted that also of interest is to identify whether or not people are likely to change their minds when truly faced with a life limiting illness. To this end, a study is underway in collaboration with the NCC to survey stage 4 cancer patients and identify whether their subsequent treatment decisions are consistent with the survey results. Other research areas that LCPC staff are actively pursuing concern the role of advanced care planning and how it can be improved and adapted for the Singapore context, ethical and policy aspects of end-of-life care, communication between patients and health care providers regarding end-of-life care issues, and identifying different strategies for financing end-of-life services. “Ultimately,” said Dr. Finkelstein, “End-of-life care is about providing the right services at the right time at the right place and for the right price. Our mission is to provide research and education in efforts to ensure those goals are met.”

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## Learning from Ezzy, a Cancer Patient

The process of learning medicine is not just from books and doctors, but from the patients we meet as well. I had a strong impression of this when I recited the Hippocratic Oath on entering medical school. It resonated when I experienced one of my most profound lessons that came not from a medical mentor; but rather, from Mr. P.H. Wang. Known to friends as Ezzy, he had outlasted a rare cancer that had taken his right leg.

Ezzy strode into the room with a welcoming smile and the confidence and balance that matched the crisp collar of his shirt and tie. His first PowerPoint slide read simply: "It's not Easy being Ezzy". Ezzy, a 44-year old former insurance professional, who loves being outdoors and living an active life and still runs and cycles, shared his story about the time when pain and grinding started to creep into his hip. Ezzy eventually ventured with unease and uncertainty to the hospital where a doctor diagnosed him with Synovial Chondromatosis: a disease of the pelvis caused by the leakage of calcium. Ezzy spoke of the surgery that was recommended for him with little warning or caution of the challenges of recovery he would experience and how it would affect the physical activities so important to him. His voice was unflinching as he told us how the pain resurfaced and how that same doctor dismissed his growing worry, shrugging off his questions. A second opinion at another hospital would reveal cancer.

Ezzy paused and said his disappointment, outrage and sadness came not from the misdiagnosis, but the unsympathetic, un-empathetic and dismissive treatment by those first clinicians. What he sought for was the care and acceptance of his pain by his doctor- not merely their clinical competence. He found this support in our clinical tutor at the National Cancer Centre Singapore.

Months later, Ezzy's words came back to me. Taking a history of a Standardized Patient, someone trained to portray a patient with a medical condition, is an exercise many medical trainees go through in their first year. In my case, Mrs. Koo had come in with a complaint of bloody urine and discomfort in her bladder. From my perspective, the interview was going smoothly and I proceeded efficiently down the long checklist of questions required for a complete medical history.

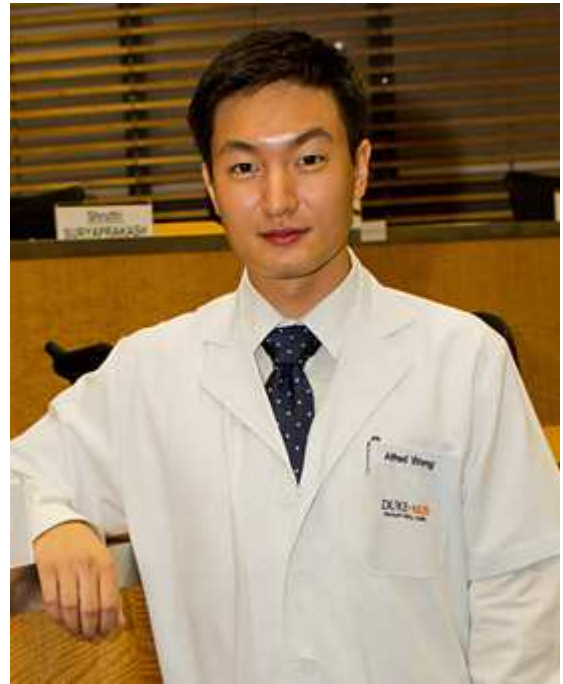
However, as the interview progressed into her social history, Mrs. Koo's mood and expressions became distressed and frustrated. She finally burst out, "Doctor! Why is it you ask me these questions? I don't understand why this has anything to do with why I am here! I came to see you, Doctor, to find out why I am having these things!" I was floored. What happened?

We had already covered what was, in my mind, all the clinically relevant aspects regarding her complaint. What did I do wrong? I had also explained the nature and importance of a social history: to guide treatment decisions down the road. Was she being deliberately difficult? Then I remembered Ezzy. I stopped and put down my checklist. I realized that I had prioritized the checklist instead of her. I prioritized my own need to be efficient and thorough instead of her need for assurance and understanding.

I looked up right at Mrs. Koo and repeated slowly and softly, "It's okay... it's okay... Mary, we do not

have to go through these questions right now. I know that you have been feeling scared of the symptoms you've been having and that you are most worried that it could be cancer. Be assured that we will be running tests to see if it is cancer. We are here to help you... are you okay?" She nodded silently and we finished the interview. I was completely drained though this was only practice. My observing clinician, Dr. Koo Wen Hsin reminded me that there are two objectives for a doctor: to build a rapport and to obtain the history. Dr. Koo offered that an incomplete history can always be filled in later; but a doctor only has one chance to build a relationship.

With many years of training ahead, many of my colleagues and I will often reflect on the challenges in practicing medicine. Frankly, I think the compassionate doctor that we all aspire to be is most vulnerable to the realities and demands of today's medical practice. I think it is too easy to be absorbed by the realities of overcrowded wards, a constant lack of time, an overreliance on checklists and technology and too little of our presence for the people around us seeking our help. We must acknowledge the burnout and depression that comes from pushing ourselves beyond healthy limits, which may cause us to shut out the emotions our patients want so desperately for us to accept. As we complete our transformation to clinicians, this acceptance is one we must grow and protect. Only if we remember Ezzy and continue to practice compassion can we, after witnessing suffering, death and disappointment, be complete as healers.



*Alfred Wong, MS 1*

Alfred Wong is a first-year MD student from the Class of 2016

For more student stories, please visit: <http://www.youtube.com/user/InsideDukeNUS?feature=watch>

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## Reflections of a First-Year MD /PhD Student

When I first started my undergraduate studies in Pharmacology at University College London (UCL), the idea of postgraduate studies was a faraway thought. My priorities then were to maximize my experience with life and studies overseas, and having good exposure in the biomedical field. I had always wanted to pursue research, and my time spent in UCL strengthened this thought even more. As my final year began, the time for choosing my future finally arrived. What did I want to do?

I definitely wanted to get into research, and after seeking advice from UCL seniors and faculty, it seemed that a PhD was my next step. But there were nagging thoughts. Was research all that I wanted to do? Was there anything I could do that would make me a better researcher? At the same time though, I had long been nursing intentions to do medicine. The completion of my degree reignited that passion. How could I then combine both these interests together: to serve patients and aid in their recovery and to understand and develop new possibilities in medicine? Thus the question became: What would enable me to do both?

My option then became a dual medical degree and a doctorate. The idea of a doctor who did research while seeing patients at the same time was not a common notion especially in our region. I would possibly have to take either one of the courses first. I knew that the idea of a clinician-scientist training program was more accepted in the US and I have heard of Duke-NUS. After looking through their website, I was excited to see that an MD-PhD program was actually available. One word rang in my head: "Perfect".

My initial concern was whether the school could provide me with the necessary skills, knowledge and experience to fulfill my goal. There were undeniable strengths: Duke-NUS partnered SingHealth, a major player in healthcare in Singapore. With many of the teaching faculty being senior clinicians, I would have access to top-notch clinical training, especially for the local context, which was ideal since I intended to practice here. I also found that Duke-NUS offered highly varied research interests, thus providing broad future research opportunities.

Moreover, with numerous top-notch researchers, I was convinced that the school is an excellent choice.

Being accepted by Duke-NUS also meant that I would be able to return to Singapore. One of the biggest draws for me to return was to do my postgraduate studies close to my family. The years apart had made me aware that old age was something that was inevitable, and I fully wished to support my parents through theirs. Although technology has made communication easy and



*Md Fadhli Bin Masri, first-year MD/PhD student and a Shaw scholar*

convenient, nothing could beat being wrapped up in the warmth of my family.



*As part of his first-year training, Md Fadhli practices with standardized patients in taking record history*

When I was informed that not only was I accepted by Duke-NUS, but also the Shaw Foundation Scholars Program, I felt truly blessed and reassured. This greatly affirmed me of the career decision, and I remain very grateful to the Shaw Foundation for the honor and privilege.

Looking back, completing the application was the only easy part. The curriculum at Duke-NUS is undoubtedly rigorous, but the amount of knowledge and experience accumulated has been enriching and invaluable in my future career.

Furthermore, my Duke-NUS course-mates come from different walks of life and their willingness to share their experiences is something I greatly cherish.

Learning in the school centers on team-based learning, which allows us to reinforce each other's knowledge and understanding. At the same time, the sharing of our past specialties and the differing opinions within the team has made us more aware and appreciative of different societal perspectives. We also gained new knowledge such as Finance, Accounting and Traditional Medicine.

After five months at Duke-NUS, I must say I am extremely appreciative and thankful for the opportunity I have to be here. The past months have been far from easy. I am not afraid to admit that I have had to study harder these past months than I had to, in my entire life. Despite this, I have not once looked back on my decision.

Mohamad Fadhli Bin Masri is a first-year MD/PhD student at Duke-NUS.

For more student stories, please visit:

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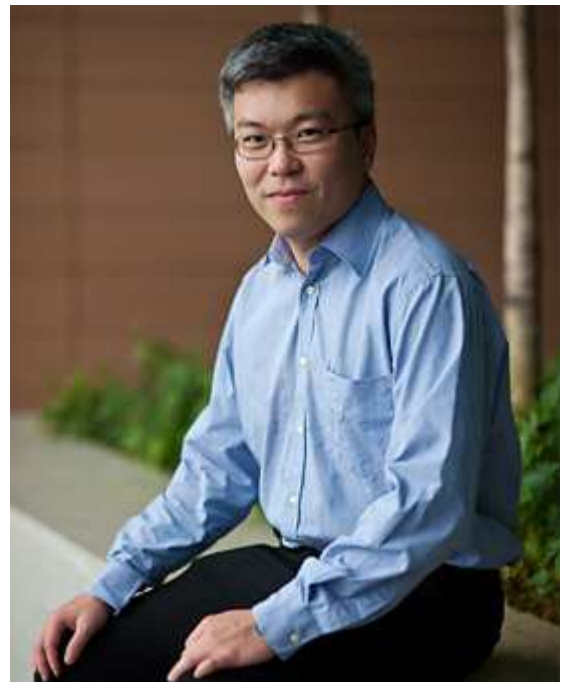
## Life After Duke-NUS

It has been more than a year since I graduated from Duke-NUS. For the past year, I was in the transition year residency program, putting in long hours and surmounting the many potentially traumatic calls. It was a year of literally backbreaking but rewarding training which took me through rotations such as general surgery, internal medicine, emergency medicine, obstetrics and gynecology. Despite all this, graduation paradoxically still feels like it happened yesterday.

On introspection, perhaps it is because I am a SingHealth resident which puts me in continued contact with Duke-NUS, her students, most of my classmates as well as our Duke-NUS clinical faculty. Residency feels like a seamless continuation of my education at Duke-NUS. This also shows the high level of integration our students have with clinical teams, the graded responsibility, close interaction and supervision by our clinical faculty such that the transition from student to resident is smooth.

Starting out in my transition year, well-armed with four years of Duke-NUS medical education, I quickly realized that knowledge is no substitute for clinical experience. While knowledge is essential, clinical experience demonstrates that not all knowledge is the same. In general, medical education seeks to expose medical students to the entire domain knowledge of medicine, on facts, numbers and even obscure data. But it was after graduation, as a medical resident, that I quickly learned that it was more important to have knowledge of commonly encountered conditions and treatment protocols close at hand. Good people skills with patients and nurses became crucial for surviving a call. After all, uncommon ailments can always be looked up, and diagnostic blind-spots identified by the team or by decision support algorithms.

Despite going through three graduation ceremonies (two were for my engineering degrees, and the third for my medical studies), I'm still far from being fully trained. Since July 2012, I started my first year of radiology residency. My initial concern regarding the loss of patient contact was well compensated by the diagnostic and intellectual challenge in radiology. As a radiology resident, training is like a trip back to the days of a medical student where I have to quickly assimilate huge amounts of knowledge and overcome the steep learning curve in acquiring a new set of skills. The case-mix and learning opportunities were plentiful, given the high clinical load that is unique to training in SingHealth. I am currently training under the supervision of dedicated consultants who never fail to challenge and encourage me.



*Dr. Chia Ghim Song, Duke-NUS MD Graduate (2011)*

Besides Radiology, I am active in the Singapore Medical Association (SMA). I chair the SMA doctors-in-training committee and together with the committee members, we are bound by the common vision of helping fellow house officers, medical officers, registrars, basic and advance specialty trainees and residents alike, be the voice and address concerns faced in the course of our daily work. This helps us serve patients at our best while we train in a reasonable and safe environment.

***“Becoming a doctor goes well beyond knowing how to diagnose and treat a patient. It is also about knowing how to wield this privilege responsibly.” - Dr. Chia Ghim Song, 1st year Radiology resident at SingHealth, Duke-NUS MD graduate (2011)***

Since graduating from Duke-NUS, my clinical experience made me understand and appreciate the value of our curriculum. Although compressed and compact, the holistic four-year education emphasized not just clinical knowledge but also the important skills of doctoring such as communication, ethics, professionalism and research, which put our graduates on a trajectory to become future change agents. As second-year medical students, it was difficult for us then, to appreciate the ethics course, especially while we were in the midst of clinical rotations.

However, since joining the profession, working in the wards and volunteering my time in the SMA, I soon found myself often drawing upon the pearls of wisdom that our faculty Dr. Thirumorthy imparted. Becoming a doctor goes well beyond knowing how to diagnose and treat a patient. It is also about knowing how to wield this privilege responsibly.

I look forward to continue giving back to Duke-NUS. As an alumnus, I see myself actively involved in teaching her students and working closely with the alumni to strengthen and advocate for Duke-NUS. In so doing, help position Duke-NUS to effect positive changes to medical education, training and by extension, the Singapore healthcare system.

Dr. Chia Ghim Song is a first-year Radiology resident at SingHealth and Duke-NUS MD Graduate (2011).

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## NEWS IN BRIEF

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## PM Lee Visits Duke-NUS

Prime Minister Lee Hsien Loong, together with Minister of Health, Mr. Gan Kim Yong, Minister of Education, Mr. Heng Swee Keat and 2nd Minister for Home Affairs and Trade & Industry, Mr. S Iswaran visited the Duke-NUS Graduate Medical School on Thursday, December 6, 2012.

Hosted by Mr. Tony Chew, Duke-NUS' Governing Board Chairman, PM Lee and the Ministers were briefed on Duke-NUS' progress by its Dean, Prof. Ranga Krishnan. They were also briefed by Prof. Robert Kamei (Vice Dean, Education) and Prof. Patrick Casey (Senior Vice Dean, Research). Our visitors were very engaged and took immense interest in the school's education methodology and research achievements and capabilities.

After the presentations, PM Lee and the Ministers toured the Emerging Infectious Diseases (EID) research laboratories, led by Program Director Linfa Wang. The EID is one of Duke-NUS' five Signature Research Programs and one of the program's key projects is anchored on a drug treating dengue fever.

PM Lee also got to observe a TeamLEAD session taking place via video stream and even had the opportunity to participate in this innovative and interactive learning style as Prof. Kamei and his team demonstrated how students' answered questions using a mobile phone app. TeamLEAD has been so successful that it is being implemented back at Duke University in North Carolina and other Ivy League institutions.

The visitors then left the Amphitheatre and met with students from the Class of 2016 in the TeamLEAD room. The students were enthusiastic and lively as they mingled and chatted with the PM and Ministers.

It was a fruitful visit and we believe the Prime Minister and his Ministers have gained a deeper insight into key Duke-NUS developments and how the school is helping to transform medicine and improve lives.

**View gallery:**



PM Lee and the Ministers with the Duke-NUS M.D. Class of 2016.



Mr. S Iswaran (far right) and Mr. Gan Kim Yong (right) having a light-hearted moment with the Welcome party comprising of (L-R) Mr. Kai Nargolwala (Duke-NUS Governing Board Member), Mr. Tony Chew (Chairman, Duke-NUS Governing Board), Dean Ranga Krishnan, Prof. Satku K (Director of Medical Services, MOH) and Prof. Tan Chorh Chuan (President, NUS).



The Welcome Party receives PM Lee Hsien Loong upon his arrival. On right: President (NUS) Prof. Tan Chorh Chuan.



PM Lee and the Ministers sharing their views.



EID Program Director, Prof. Linfa Wang explains to PM Lee about the research program as the Ministers look on.



(L-R) Dean Ranga Krishnan and Prof. Kamei explains the TeamLEAD concept to our guests.



PM Lee having a go at the mobile app Duke-NUS students use to participate in TeamLEAD sessions.



PM Lee having a chat with students in the TeamLEAD room.



Seated (L-R): Mr S Israwan, Mr. Gan Kim Yong, Mr. Tony Chew, PM Lee Hsien Loong, Mr. Heng Swee Keat, Mr. Kai Nargolwala, and Prof. Tan Chorh Chuan. Standing - Ministry & Duke-NUS senior leaders (L-R): Dr. Lau Hong Choon, Ms. Karen Chang, Prof. John Rush, Dean Ranga Krishnan, Prof. Patrick Casey, Prof. Robert Kamei, Prof. Satku K, and Mr. Roy Quek.

## New Institute for Research Launched

Following the launch of the Academic Medicine Education Institute (AM•EI), the Academic Medicine Research Institute (AMRI) was launched on Nov 5, 2012. It was attended by guests from across disciplines in Duke-NUS and SingHealth. Themed after Star Wars, 'jedis' presided over the launch followed by talks by Dean Ranga Krishnan, Prof. Soo Khee Chee, Prof. Ivy Ng, Prof. Wong Tien Yin and Prof. John Rush.



*Prof. Soo Khee Chee sharing about AMRI*

The AMRI is a collaboration between Duke-NUS and SingHealth, in providing scientific support to help develop research careers of budding and established clinicians investigators, clinician scientists and the other researchers in the Duke-NUS/SingHealth Academic Healthcare Cluster. AMRI fosters collaborations among scientific, clinical and quantitative experts in the Academic Clinical Programs (ACPs) and helps researchers to develop their ideas into research proposals, attain grants, execute projects and publish their findings. AMRI provides mentoring, facilitates development of collaborations and supports pilot studies. AMRI has two branches – one at KKH and another at SGH.

Executive Director of AMRI and Vice-Dean Clinical Sciences, Prof. John Rush sums up the AMRI simply as “AMRI provides scientific support to healthcare researchers through collaborations with quantitative, health services and clinical research expertise, and linkages to laboratory-based investigators. AMRI develops tools such as Voice Annotated Presentations and processes such as interactive research development seminars, grant pre-submission reviews, medical editing, pilot awards and other programs.”

For more information on Academic Medicine, please visit: [www.duke-nus.edu.sg/academic-medicine](http://www.duke-nus.edu.sg/academic-medicine)



*The AMRI is launched (L-R): Prof. John Rush, Prof. Wong Tien Yin, Dean Ranga Krishnan, Prof. Ivy Ng, Prof. Patrick Casey & Prof. Soo Khee Chee*



*Prof. John Rush trying his luck at a 'Spin & Win' wheel*

## Recognizing Research Excellence: The National Medical Research Council Awards

The 2012 National Medical Research Council (NMRC) Human Capital Awards recognized 25 clinician scientists from seven healthcare institutions for their innovative research in the pursuit of quality healthcare and better patient outcomes.

The NMRC Awards – comprising the Singapore Translational Research Investigator (STaR) Award, Clinician Scientist Award (CSA) and Transition Award – were given to researchers in a range of fields that spanned Cardiology, Mental Health, Neurology and Infectious Diseases. Of the 25 awardees, eight recipients currently hold Duke-NUS appointments. They include STaR award recipients Professors Stuart Cook and Karl Tryggvason, CSA recipients Professor Cheung Yin Bun and Assistant Prof. Ling Khoon Lin. Transition awards were given to Assistant Prof. Jimmy Lee, Dr. Chong Tsung Wen, Dr. Leung Ying Ying, and Dr. Charumathi Sabanayagam. Congratulating the awardees, Mrs. Tan Ching Yee, Permanent Secretary (Health), said, “Investment in research is important for the future, as the new knowledge created helps us to better respond the multiple challenges facing healthcare.”

### **STaR Award: Stuart Cook (NHCS and Duke-NUS)**

Professor Cook is a Distinguished Clinician Scientist, Senior Consultant in Clinical and Molecular Cardiology and Senior Research Advisor with the Department of Cardiology at the National Heart Centre (NHC) Singapore and is a Professor at Duke-NUS’ Cardiovascular and Metabolic Diseases Research Program, where he has established a laboratory.



*Prof. Stuart Cook*  
*Photo: Tomorrow's Medicine, SingHealth*

Over the last five years, Professor Cook and his team have identified a number of new genes for heart and artery diseases – the most common cause of death and disability worldwide – to prevent, diagnose, stratify and treat cardiovascular disease.

Using state-of-the-art approaches that integrate advanced cardiac imaging with genomic data, Prof. Cook has derived novel insights into these diseases. His work is also driven in part by the advances in human genetics in the post-Human Genome Project era and, more recently, the availability of ultra-high throughput sequencing technologies, such as those at Duke-NUS.

Some of his work in Singapore includes working with the National Heart Centre Singapore (NHCS) to investigate why some abnormal heart rhythms that lead to strokes occur; developing research into clinical diagnostic tools for sudden cardiac death; and understanding healthy cardiovascular ageing.

His work has been published in *Nature* and *Nature Genetics* as well as the *New England Journal of Medicine*.

### **STaR Award: Karl Tryggvason (Duke-NUS)**



*Prof. Karl Tryggvason*

Professor Tryggvason is a Professor in the Department of Medical Biochemistry and Biophysics at Karolinska Institutet in Stockholm and in the Cardiovascular & Metabolic Disorders Program at Duke-NUS.

His work in understanding the role of basement membrane proteins in normal physiology and disease has led to numerous discoveries in the area of glomerular epithelial cell or podocyte in human glomerular disease as well as understanding the molecular basis of other

non-renal basement membrane diseases.

Some major discoveries have been in understanding the molecular features of the filtration barrier in the kidney; determining the causes of human kidney diseases such as congenital nephrotic syndrome; and forming the research basis for understanding junctional epidermolysis bullosa and



congenital muscular dystrophy. More recently, his laboratory has developed methodologies for synthesizing laminins, a family of basement membrane proteins, and has shown that these proteins can be used to control stem cell growth and differentiation.

At Duke-NUS, Professor Tryggvason plans to build a program focused on understanding the causative mechanisms of diabetic nephropathy, the leading cause of end-stage kidney disease in Singapore.

### **Transition Award: Jimmy Lee (IMH, Duke-NUS)**

Dr. Lee is a Consultant Psychiatrist with the Department of General Psychiatry 1 and Research Division at the Institute of Mental Health and Assistant Professor with the Office of Clinical Sciences at Duke-NUS.

His work in demonstrating the potential of blood-based biomarkers in identifying individuals with schizophrenia hopes to develop more a reliable and objective diagnostic approach so as to make earlier, more accurate diagnosis to ensure early interventions. This new approach will also improve assessments following treatment.



*Dr. Jimmy Lee received his award from Guest-of-Honor Mrs. Tan Ching Yee, Permanent Secretary (Health)*

Dr. Lee and his team has attempted to reproduce the same results from earlier studies in a larger sample and looking to evaluate the ability of these blood-based biomarkers in predicting clinical outcomes, particularly in relation to selecting suitable therapeutic regimens. If successful, this will be a significant advancement in the management of psychosis, as a biomarker will provide objectivity to evaluate disease responses and assessing the right treatment plans.

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## **Fostering the Spirit of Giving**

Duke-NUS is launching its inaugural Annual Giving Campaign to bring faculty, staff and students together.

Individuals and teams are challenged to do something for a Duke-NUS cause they are passionate about. Whether it is to stretch one's physical limits or to achieve a goal, the campaign aims to rally colleagues and friends to support and celebrate the ability to give; because we believe in transforming medicine and improving lives.



### 3 ways you can participate in the Annual Giving Campaign:

- 1) Sign up as a champion and start garnering support for your cause. More details on how to sign up as a champion can be found below.
- 2) Join a [Public Challenge](#) by making a donation to any Duke-NUS [cause](#).
- 3) Support our Champions by donating to their cause, or simply make a donation to any Duke-NUS [cause](#).

#### Sign up as a Champion

Step 1: Select an [existing cause](#), or propose a new cause.

Step 2: Select a [Public Challenge](#), or design your own personal challenge.

Step 3: Set a target amount you hope to raise.

Step 4: Tell your story to inspire support for your cause!

For more information, please visit: [www.duke-nus.edu.sg/annualgiving](http://www.duke-nus.edu.sg/annualgiving)

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## RESEARCH NEWS

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- ▶ Genetic Deletions in Y-Chromosome Contribute to Male Infertility
- ▶ Epigenetic Analysis of Stomach Cancer Finds New Disease Subtypes
- ▶ Brain-Computer Interface Program Shows Promise for Treating ADHD
- ▶ Fat-Regulating "Master Protein" Identified
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## Researchers Find Genetic Link Between Bats' Ability to Fly and Viral Immunity

An international team led by an infectious disease expert, Professor Lin-Fa Wang has found that the evolution of flight in bats may have contributed to the development of a highly effective immune system, allowing bats to harbor some of the world's deadliest viruses such as Ebola and SARS.



*The black flying fox, Pteropus alecto*  
Photo credit: Susanne Wilson/CSIRO AAHL

In their study, published in the prestigious international journal *Science*, Professor Wang and colleagues used a state-of-the-art whole-genome sequencing technique to analyze the genomes of two distantly-related bat species, the fruit bat *Pteropus alecto* (Black flying fox, a species native to Australia, Papua New Guinea, and Indonesia) and the insect-eating bat *Myotis davidii* (David's mouse-eared bat, a species endemic in China).

"This is the first in-depth study of bat genomes. Our study provided important genomics insights into the unique biological features of bats," said Professor Wang, an expert in bat-borne viruses who was appointed Director of the Program in Emerging Infectious Diseases in July last year.

The large collaborative team from China, Denmark, Australia, U.S., and Singapore compared the two bat genomes with the genomes of other mammals, and found genetic clues that may account for the unique characteristics of bats.

Although bats are the second largest group of mammals, with over 1,000 species of bats documented so far, they are distinctive because they are the only mammals capable of sustained flight; other mammals such as flying squirrels glide but do not fly.

Previous research has shown that this ability to fly may be linked to high metabolic rates in bats. However, increased metabolism also elevates the amount of free radicals in living cells, resulting in DNA damage that is harmful to the bats.

Through their analysis of bat genomes, the researchers have now solved the mystery of how bats tolerate high levels of free radicals. It appears that bats have evolved mechanisms to overcome this toxic side-effect of flying, as they possess gene variants that help them minimize and repair DNA damage.

And here is where bats' ability to fly and their immunity against viruses intersect: the same gene variants that minimize DNA damage in bats may also provide protection against viruses, boosting their innate immune system to ward off such attacks.

Having a highly active immune system may explain why bats are natural hosts of many viruses such

as Hendra, Nipah, Ebola, and SARS, yet rarely show any signs of infection. In contrast, when these viruses are transmitted to humans or other animals, the resulting illness is often severe and even fatal.



*Prof. Linfa Wang*

Bats are also known for their exceptional longevity which is unusual because of their small size and high metabolic rate. The researchers raise the intriguing possibility that the same mechanisms underlying the evolution of flight and viral immunity in bats may also be responsible for their life expectancy, although further research is required to establish this link.

Professor Wang hopes that the findings from this study will provide new research directions into infectious diseases, especially in the treatment, prevention, and control of emerging infectious diseases that affect both humans and livestock animals.

"Our findings highlight the potential of using bats as a model system to study infection control, tumor biology, and the mechanisms of aging," said Prof. Wang, who intends to continue studying bat-borne viruses, tapping on Duke-NUS' strengths in human infectious disease research for viral diseases such as dengue and influenza, and to explore new collaborative research in tumor biology with scientists in the Cancer and Stem Cell Biology Program here.

Professor Wang is also a Science Leader for the CSIRO Office of the Chief Executive and Senior Principal Research Scientist at the CSIRO Australian Animal Health Laboratory (AAHL) in Geelong, Australia.

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## **Inhibiting 'Porcupine' Enzyme Potential Treatment for Certain Breast Cancers**

Early stage animal studies have found that inhibiting an enzyme known as PORCN may prevent growth of certain cancers. Lead researcher Professor David Virshup, Director of the Program in Cancer and Stem Cell Biology at Duke-NUS, explained that the study tested if an enzyme important in development and in stem cells might make a good cancer drug target.

"The enzyme we targeted has the entertaining name of 'porcupine', so named because it was discovered in basic research in *Drosophila* (flies). It's called PORCN for short," Prof. Virshup explained. "PORCN plays an important role in the Wnt signaling pathway (responsible for cell-cell communication and growth control). We know that all 19 human Wnts require PORCN for their activity, suggesting that inhibition of PORCN could be an effective treatment for cancers dependent on excess Wnt activity." Mutations in Wnt signaling pathways are found in many cancers as well as other diseases.



*Prof. David Virshup in discussion with his lab members*

In the study, the team used a drug called C59, originally developed by Novartis. “We wanted to see if the drug inhibited PORCN, if it blocked the production of active Wnts in the body, and finally if it blocked Wnt-dependant cancer,” said Prof. Virshup. The study found that the drug was very good at treating cancer in a mouse model and more significantly, that it was not toxic at an effective dose. The results were published in November 2012 in the journal, *Cancer Research*. “This suggests people with cancer can tolerate the drug, and it may be useful in specific kinds of cancer,” added Prof. Virshup. “The work is about the proof of concept of a new class of cancer drugs and is the first publication to show such a drug can work in an animal.”

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## **Genetic Deletions in Y-Chromosome Contribute to Male Infertility**

A study of more than 20,000 men has found that two spontaneously recurring deletions along a complex region of the Y-chromosome are responsible for about 8 per cent of cases of failed sperm production.

The study, conducted by Steven Rozen, an Associate Professor at Duke-NUS Graduate Medical School Singapore and first author of the study in collaboration with Whitehead Institute Director David Page and colleagues has shown that severe spermatogenic failure (SSF) is caused by genetic deletions in the region of the Y-chromosome known as the AZFc (for azoospermia factor c) region. The deletion known as b2/b4 is found in one of every 2,300 men, and it increases the risk of SSF by 145 times.

Associate Prof Rozen noted, “Medically relevant population genetics studies are well established for most of the human genome, but this is the first study of this kind for the Y-chromosome.” The study also relied on a unique sequencing method developed by Rozen and Page to help navigate the structural complexities of the Y-chromosome. The study was published in the *American Journal of Human Genetics* in November 2012.

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## Epigenetic Analysis of Stomach Cancer Finds New Disease Subtypes

A team of researchers at Duke-NUS, led by Professor Patrick Tan has found that gastric cancer is not just one single cancer but a cluster of many different cancer types, some of which are triggered by bacteria or gastric inflammation. The researchers also found that some of these newly identified subgroups of cancer (known as CpG island methylator phenotype or CIMP tumors) – which form third of all gastric cancer cases – have extremely high levels of methylation. These cancers tend to present in younger patients and indicate a poorer outcome. These discoveries throw significant light into understanding how to better diagnose, target and treat gastric cancer, which is the second most deadly cancer in the world after lung cancer.

Professor Tan explained, “These results provide further confirmation that gastric cancer is not one disease but a conglomerate of multiple diseases, each with different underlying biologies and hallmark features ... If gastric cancer is the result of multiple interacting factors, including both environmental factors and host genetic factors, we need better ways to diagnose and treat it.”

In the study, the team analyzed 240 primary tumors and cell lines to determine the various methylation profiles of gastric cancers. Methylation is a chemical process in which specific locations along the DNA, (at areas called CpG sites) are modified through the addition of a methyl group. Methylation silences a gene's behavior without actually altering the DNA sequence. Methylation – unlike genetic mutation – is an external or epigenetic alteration.

The team's goal was to identify new molecular subgroups of gastric cancer not caused by primary genetic mutations but epigenetic (external) alterations – and identify the subgroups that can be better diagnosed and targeted.

Understanding methylation patterns means simple diagnostic test can be potentially developed to detect gastric cancer at earlier stages in the disease, said Prof. Tan. “Our study does provide clarity in unambiguously demonstrating the presence of this subgroup and its features ... What's more, we are encouraged that there may be potential utility in testing the sensitivity of CIMP tumors to more potent DNA demethylating agents and possibly other epigenetic drugs.” added Tan, who is also affiliated with Singapore's National Cancer Centre and the Genome Institute of Singapore.

The study, funded by the Singapore Gastric Cancer Consortium and allied grants, was published in the journal *Science Translational Medicine* in October 2012.



Prof. Patrick Tan

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## Brain-Computer Interface Program Shows Promise for Treating ADHD

A brain-computer interface (BCI)-based training program has been found to have promising outcomes as a treatment for Attention Deficit Hyperactivity Disorder (ADHD). The joint study was conducted by the Institute of Mental Health (IMH) in collaboration with the Institute for Infocomm Research (I2R) – a research institute of the Agency for Science, Technology and Research (A\*STAR) – and Duke-NUS.

The study involved 20 children aged 6 to 12 years old with ADHD not receiving any medication for their condition. During an eight-week period, the children received training through a BCI-based game system three times a week. They wore a headband with electroencephalography (EEG)



*A child engaged in intervention with the BCI attention training game system*

sensors while they 'played' with a computerized 3D graphic game developed by I2R. In this game, the child controlled an avatar by focusing their thoughts and the signals picked up via the EEG electrodes moved the avatar. The BCI-system also measured the attention level and proportionally increased or decreased the game speed accordingly. The greater the concentration level, the faster the speed of the avatar's movement. At the end of every alternate training session, academic tasks were also given to train the child to learn to focus in the same way as during the game. The results

showed that both parent-rated inattentive and hyperactive-impulsive symptoms on the ADHD Rating Scale showed significant improvement – in particular in children with more severe symptoms.

The study was led by Principal Investigator, Dr. Lim Choon Guan, Consultant and Deputy Chief from the Department of Child & Adolescent Psychiatry, IMH. Co-Principal Investigators included Associate Professor Daniel Fung, Chairman Medical Board and Senior Consultant from the Department of Child and Adolescent Psychiatry, IMH, Prof. Ranga Krishnan and Associate Professor Lee Tih-Shih from Duke-NUS, Dr. Guan Cuntai, A\*STAR's Institute for Infocomm Research, and Prof. Cheung Yin Bun and Dr. Zhao Yudong from the Singapore Clinical Research Institute.

Dr. Lim noted how this was a promising new way to treat ADHD without drugs, "Many parents prefer to train their children to overcome their difficulties rather than rely on medication but find behavioral management strategies hard to implement or deliver results. We are excited by this early result as it points to a potentially new and effective way to treat children with ADHD."

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## **Fat-Regulating "Master Protein" Identified**

Obesity is widely recognized as a serious global health threat. Obesity can lead to the development of a number of chronic diseases, such as diabetes, heart diseases and cancer. An international collaborative study involving Duke-NUS researcher, Dr. Jit Kong Cheong (Cancer and Stem Cell Biology Program), and researchers from the United States, Spain, France and Germany, have identified a protein named TRIP-Br2, a transcriptional co-regulator, as a crucial regulator of body weight. The team discovered that mice lacking the TRIP-Br2 gene did not gain weight no matter what they ate — even when placed on a high-fat diet — and were otherwise normal and healthy. "It turns out that this protein coordinates expression of a lot of genes and controls the release of the fuel form of fat and how it is metabolized," explained Professor Stephen Hsu I-Hong (University of Florida), a co-senior author of this study. "It is still early days but this discovery could aid the development of drugs that targets multifunctional proteins like TRIP-Br2.", said Dr. Cheong. Ongoing research will provide insights to what actually triggers the expression of TRIP-Br2 and whether these findings in mice can be translated to humans.

The study was published online ahead of print in the journal *Nature Medicine* on January 6.

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## **Two Duke-NUS Faculty Elected AAAS Fellows**

The American Association for the Advancement of Science (AAAS) has elected 702 new members for its new 2012 class of fellows, which include 14 members of the Duke faculty.

The AAAS appointment is a mark of recognition of peers in the field who have made scientifically or



*Patrick Casey, Senior Vice Dean (Research)*

socially distinguished efforts to advance science or its applications.

Among the 14 AAAS fellows from Duke, two are from the Duke-NUS faculty. Their election is a strong mandate from the international scientific community on the excellent scientific leadership in the graduate medical school.

**Patrick Casey, Senior Vice Dean (Research)** - For distinguished contributions to the fields of biochemistry and pharmacology, particularly in the study of protein modifications and their impact on cellular signaling processes.

**Soman Abraham, Professor, EID Program** - For distinguished and pioneering contributions to the elucidation of mechanisms of bacterial pathogenicity and host immune responses, particularly the important role of mast cells.

New AAAS fellows will be presented with an official certificate and a gold and blue (representing science and engineering, respectively) rosette pin on Saturday, February 16, 2013 at the AAAS Annual Meeting in Boston.

This year's AAAS Fellows were formally announced in the November 2012 edition of the journal *Science* in the AAAS News & Notes section. Besides Profs. Casey and Abraham, six fellows associated with Duke University Medical Center were also elected.



*Soman Abraham, Professor, EID Program*

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HOME ► GRANTS AWARDED

## GRANTS AWARDED

- ▶ Developing a fiber-optic endoscopic microscope to image neurosecretion in intact mouse brain in vivo
- ▶ Genetic susceptibility, animal models, biomarkers and therapy of diabetic nephropathy, and differentiation of human stem cells with human laminins
- ▶ EEG-Based Brain Computer Interface for cognitive Enhancement in Elderly with age-related Cognitive decline and mild cognitive impairment (3E-COG)
- ▶ Developing Clinically implementable multiplex gene assays for specific indications across the continuum of care in stomach and kidney cancer
- ▶ Cancer Patients & Their Caregivers: Perspectives on Collusion, Quality of Life and Treatment Cost

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Details of projects awarded to Duke-NUS researchers from Sep-Dec 2012

No.	PI	Dept	Project Title (Please click titles for details)	Grant Call	Duration (Months)
1.	Hyunsoo Shawn Je	NBD	Developing a fiber-optic endoscopic microscope to image neurosecretion in intact mouse brain in vivo	NUS Cross Faculty Research Grant Call	24
2.	Karl Tryvaggson	CVMD	Genetic susceptibility, animal models, biomarkers and therapy of diabetic nephropathy, and differentiation of human stem cells with human laminins	NMRC STAR Award	60
3.	Lee Tih Shih	NBD	EEG-Based Brain Computer Interface for cognitive Enhancement in Elderly with age-related Cognitive decline and mild cognitive impairment (3E-COG)	Biomedical Engineering Programme 2011	18
4.	Patrick Tan	CSCB	Developing Clinically implementable multiplex gene assays for specific indications across the continuum of care in stomach and kidney cancer	Bedside and Bench Dec 2011 Grant Call	36
5.	Sumytra Menon	Lien Centre	Cancer Patients & Their Caregivers: Perspectives on Collusion, Quality of Life and Treatment Cost	Lien Centre For Palliative Care Intramural Research Award	12

**Total Amount of Funding Received for Sep - Dec 2012: \$13,512,224.56**

## Synopsis

### **1. Developing a fiber-optic endoscopic microscope to image neurosecretion in intact mouse brain in vivo**

Hyunsoo Shawn Je, [Neuroscience & Behavioral Disorders](#)

Identifying the neural basis of behaviour is a core focus of neuroscience. Aberrant behaviors shown in neuropsychiatric diseases may involve an imbalance of neurotransmitter secretion. In particular, alteration of acetylcholine (ACh) secretion has been implicated as the underlying pathophysiology of Alzheimer's disease (AD), the fourth leading cause of death among the elderly in developed nations. Dr. Shawn Je's laboratory at Duke-NUS GMS has recently developed a brain-implantable cell-based ACh biosensor. By chronically implanting ACh sensors in the brain of mice models of AD, we can test whether alteration of ACh release in specific areas of brain correlates with abnormal animal behaviors in AD model mice. To achieve this, the laboratory of Dr. Zhiwei Huang at NUS will construct a fiber-optic fluorescence microscope, which enables minimally invasive in vivo imaging of ACh sensors in deep brain areas inaccessible to conventional microscopy. These collaborative approaches promise to provide novel insights for devastating neurological disorders.

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### **2. Genetic susceptibility, animal models, biomarkers and therapy of diabetic nephropathy, and differentiation of human stem cells with human laminins**

Karl Tryvaggson, [Cardiovascular & Metabolic Disorders](#)

Vascular complications of diabetes causing nephropathy, retinopathy, neuropathy, chronic skin ulcers and amputations, affect about 30-50 % of diabetic patients worldwide. Diabetic nephropathy (DN) accounts for 50 % of all dialysis cases. The genetic regulation and molecular pathomechanisms of diabetic nephropathy are poorly understood which hinders development of diagnostics and therapy. The project has four main objectives: (i) Generation of mouse models relevant for the exploring the human disease. Currently, there are no proper animal models for studying diabetic nephropathy; (ii) Elucidation of glomerular transcriptome profiles in human and mouse DN to gain insight into pathogenic pathways and for identifying novel drug targets; (iii) Participation in a phase 3 clinical trial for a new DN drug, where patients under treatment will be analyzed for changes in glomerular expression and examined for effects by nephrologists and ophthalmologists; (iv) Exploration of human recombinant laminins for proliferation and design of controllable differentiation protocols of stem cells to insulin-producing and other cell types. Our recent groundbreaking results on development of methods for xeno-free and feeder-free systems and monolayer culturing of pluripotent human stem cells from single cells and from single cell suspension on unique laminins form a basis for cell differentiation studies with laminins.

We will use Singapore's state-of-the-art infrastructure platforms for making and analyzing a variety of genetically modified mice, for carrying out genome and deep sequencing for studying genetic variants and transcriptome profiles of glomeruli. We will work closely with local clinicians for obtaining patient material for studying glomerular expression profiles and for studying progression or cure of patients with renal and ophthalmologic changes. The work on cellular expansion and differentiation will partially be carried out in collaboration with local scientists.

The results can have significant impact on the understanding of the underserved research on mechanisms of diabetes complications and promote drug and diagnostics development.

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### **3. EEG-Based Brain Computer Interface for cognitive Enhancement in Elderly with age-related Cognitive decline and mild cognitive impairment (3E-COG)**

Lee Tih Shih, Neuroscience & Behavioral Disorders

Subjective memory loss is the most common complaint and cognitive impairment is the most common neurological disease of the elderly. Age related cognitive decline (ARCD) and mild cognitive impairment (MCI) are recognized clinical entities that are less severe along the spectrum of normal to Dementia. Timely and intensive intervention may be useful in regaining and preserving cognitive function and even delaying dementia. With a rapidly aging population in Singapore and much of the developed world, these problems have become the greatest public health challenge. There are no evidence-based treatment options currently available for ARCD and MCI. With this pressing national need and an opportunity, engineers and scientists from I2R are working closely with clinician investigators from Duke-NUS SGH and YLLSOM/NUHS to create a novel EEG-based Brain Computer Interface (BCI) attention-memory training system that is individualized to subjects and driven by subjects' concentration and cognitive performance.

This proof-of-concept proposal is intended to study the safety, usability, acceptability and an efficacy signal of such a system. We are currently studying elderly subjects who have ARCD and MCI, totalling 44 persons recruited from the Singapore Longitudinal Aging Study (SLAS) in a randomized control trial with a wait-list control. The results from this POC will help inform on whether this system is practical and helpful and how it can be improved upon and whether and/or how to embark on a major efficacy trial.

Our eventual goal is to create a 'personalized medicine' device for regulatory approval in Singapore, USA and other major markets, consistent with national policies and needs. One U.S. based corporation has already indicated an interest in commercializing our proposed device for the US and other markets.

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### **4. Developing Clinically implementable multiplex gene assays for specific indications across the continuum of care in stomach and kidney cancer**

Patrick Tan, Cancer & Stem Cell Biology

Previous genomic research has shown that gene expression profiles (GEPs) can function as a powerful technology capable of providing biological 'snapshots' of distinct biological programs and cell types present in primary human cancers. Sufficient evidence has also been accrued demonstrating the clinical utility of measuring tumor GEPs, for molecular subtyping, predicting patient prognoses, or responses to therapy. However, despite their clinical potential, GEPs have yet to find their way into standard clinical practice. Historically, one major limitation has been the reliance of GEPs on fresh-frozen tumor materials, in contrast to the formalin-fixed paraffin embedded (FFPE) samples that represent the mainstay of standard pathology labs for decades. Recently, the Nanostring nCounter system has shown great promise as a platform for measuring GEPs in FFPE materials. In this application, we propose to apply the Nanostring system to develop and validate a panel of clinically-relevant GEPs identified from our prior analysis of gastric and kidney cancers. These FFPE-amenable multiplex assays will be validated on a series of patient populations from Singapore, USA, Japan, South Korea, UK, and USA with access to clinic-pathological information from either retrospective archives or completed clinical trials. Information from these projects will unambiguously establish the clinical utility of these GEPs, in a fashion that can be rapidly deployed into standard histopathology laboratories. Undoubtedly, there is a strong world-wide demand for accurate diagnosis for these two cancer types and prediction of drug response in stratifying the right patients for the appropriate drugs to improve their clinical management. Once validated from the studies, the assays will be protected for commercialization, either as a spin-off or in collaboration with a commercial entity. As the world leaders in these two cancer types with the largest gene expression data, we are in the best position to succeed in the

most timely and competitive manner.

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## 5. Cancer Patients & Their Caregivers: Perspectives on Collusion, Quality of Life and Treatment Cost

Sumytra Menon, Lien Centre

This study examines end of life decision-making and compares the perspectives of cancer patients and their caregivers and/or decision-makers. The research aims to better understand perspectives on the:

- role the patient, caregivers, relatives, friends and healthcare professionals play when disclosing the diagnosis of terminal cancer, and
- choice of a treatment that offers a good quality of life, versus a poorer quality but slightly longer life, where treatment is an out-of-pocket expense compared to when a treatment is not an out-of-pocket expense.

We hope this study will benefit healthcare professionals, researchers and policymakers, and raise awareness of the need for advance care planning. By exploring people's perspectives on end of life decision-making, palliative care professionals will gain further insight into collusion, quality of life, and treatment cost, thereby better equipping them to help patients and caregivers in difficult stages.

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