



## Highlights



### Bringing synergy to medical research, education and clinical care

The biggest breakthroughs in medical science combine tenacious research, dedicated clinical application and the sharing of that invaluable knowledge. Taking this synergy to a new level is a partnership between Duke-NUS and SingHealth where research is not an end to itself, but is applied...

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### A year of discovery

Since its inception in 2005, Duke-NUS has been offering a unique model of graduate medical education. Aside from imparting relevant specialty knowledge, the goal has been to encourage its students to push the boundaries of medicine.

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### Paying it forward

For Dr. Karen Nadua, her contribution to the 2011 Class Gift Fund was more than a mere donation – it was a token of appreciation for being able to fulfill her dreams.

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## The class of 2015 begins their medical journey

This year's White Coat ceremony for the fifth intake of students (Class of 2015) was held on 12 August in the College of Medicine Building Auditorium. The donning of a white coat - a symbol of becoming a member of the medical community committed to clinical service and patient care.

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- Study offers clues into the mechanism of mutation of influenza
- Identifying the complexities in dementia care

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## The music of medicine

Vital Science speaks to our resident student band, Acoustic Bop -- comprising Josh Chua, Giselle Reinoso, Apurva Thanju and Esther Low - on the harmonious twinning of Medicine and Music.

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MD Year 1 Foundations  
Course activities  
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MS3 students' research  
day  
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## FYI:



## VITAL SCIENCE

A quarterly e-newsletter produced by Office of Communications and Development  
Editorial & Production: Praise Tan, Wee Lai Ming (Duke-NUS)  
Writer: Sheralyn Tay

*This issue's banner shows our award winning students with their 3rd year research mentors. (L-R: Prof. Aung Tin, Foo Li Lian, Yong Ming Hui and Assoc Prof. Tan Eng King). Foo Li Lian received the Young Investigator Award (YIA) at the 19th SGH Annual Scientific Meeting (ASM) and Yong Ming Hui won one of three 'Best Poster Presentation' awards at the 45th Singapore Malaysia Congress of Medicine. Read about them in "[A year of discovery](#)".*

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## Bringing synergy to medical research, education and clinical care

The biggest breakthroughs in medical science combine tenacious research, dedicated clinical application and the sharing of that invaluable knowledge. Taking this synergy to a new level is a partnership between Duke-NUS and SingHealth where research is not an end to itself, but is applied and studied in the context of medical practice to improve patient care and educate other doctors.

The concept known as **Academic Medicine** integrates three functions of medicine - clinical care, education and the development of new knowledge - to close the gaps between research and academic discovery by taking it to where it matters most - patients, explained Prof. John Rush, Vice Dean of Clinical Sciences at Duke-NUS.

In Singapore, this model of medicine is being realized on Outram Campus between Duke-NUS and SingHealth, where faculty in clinical, research and education activities work with students and staff in close collaborative spirit to nurture an environment that encourages new discoveries in healthcare and patient care. The key to the partnership's success is the integration of cutting-edge research and clinical studies. In this environment, knowledge, expertise and competency in medicine is developed, shared and passed down to impact clinical care in a manner that provides cost-effective patient-centric clinical care results. This collaborative model builds on similar concepts across the world, such as the Johns Hopkins University, Imperial College Academic Health Science Centre and Duke Medicine.

"The SingHealth/Duke-NUS Academic Medicine partnership is envisioned as an integrated working enterprise that guides and promotes the future of medicine," explained Prof. Ranga Krishnan, Dean of Duke-NUS. "It taps on and combines the collective strengths of SingHealth's clinical expertise and Duke-NUS' biomedical sciences research and medical education capabilities. Shaping this vision at Duke-NUS is Prof. John Rush, who is joined by Prof. Robert Kamei who will drive the educational thrust, while Prof. Patrick Casey will lead the research partnerships."

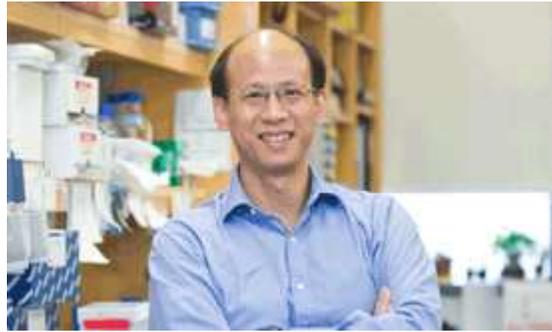
To nurture cross-fertilization, joint-appointments will be awarded to clinicians who can take on clinician-practitioner, clinician-educator and clinician-researcher roles. New Research and Education programs will cut across academic departmental structures to leverage on shared expertise and knowledge.

In integrating strengths in education and research across a shared platform, specialists in a specific field can raise questions on how to better treat an illness and rely on collective wisdom to find timely and often life-saving solutions. Prof. Rush highlighted, "Within Academic Medicine

there is a platform for collaboration between clinicians and researchers, and often these two activities are both the daily work of one person!"

## Research in motion

Highlighting the value of collaboration are several ongoing clinical and translational studies. One study, in chronic myeloid leukaemia (CML), is a collaborative effort between Dr. Ong Sin Tiong, Associate Professor in the Cancer & Stem Cell Biology Signature Research Program, and Principal Investigator in the Laboratory of Haematologic Malignancies at Duke-NUS, and Assistant Professor Charles Chuah, the lead physician for CML clinical studies, and Senior Consultant in the Department of Haematology, at SingHealth's Singapore General Hospital (SGH). The study investigates reasons for drug-resistance in CML, and identifying new drug targets to improve treatment in patients with CML.



*Assoc Prof. Ong Sin Tiong*

The partnership has given their research a competitive advantage, they said. "It's best when you have two people who are deeply interested in a particular phenomenon. It means a close working relationship clinician-scientists, who understand what the clinical issues are, and basic researchers who provide additional mechanisms-based insights," said Dr. Ong. Dr. Chuah agreed, adding that having a shared goal and frequent exchange of information has elevated the status of CML research in Singapore to an international level.



*Asst Prof. Charles Chuah*

The collaboration with SingHealth also means Dr. Ong can study a greater volume of cases at both the Singapore General Hospital and in related cancers at the National Cancer Centre. "Some of the diseases we study are very important but less common among the general population, so being at a center where these patients come to seek specialist help is a tremendous advantage," he said.

Another boon: geographical proximity to patients and other collaborators. "Within a few square kilometers, I have access to clinical collaborators, cutting-edge technologies, and whole teams of medicinal chemists (from the Experimental Therapeutic Centre in A\*Star) who are helping us design new drugs for patients. There are very few places in the world that can offer this level of synergy," said Dr. Ong, "It is really important to have people who are like-minded, so that we have a significant advantage over our competitors."

From a practical point of view, Dr. Chuah also gets the institutional support he needs. "I have been fortunate to have 70% protected time for research. This was made possible through the NMRC Clinician Scientist Award. My Head of Department and colleagues also recognize the importance of research and are very supportive of my ongoing work in terms of advice and recruiting patients into my research protocols."

Another trial on dengue vaccine has brought together Dr. Ooi Eng Eong, Associate Professor, Program in Emerging Infectious Diseases at Duke-NUS with Dr. Jenny Low, Infectious Disease Consultant at SGH. Said Dr. Ooi, "We have the best of both worlds. Dr. Low has the advanced clinical training and experience and I have the laboratory tools to examine immunity against dengue. In collaborating, we can move the clinical observations into further scientific

investigations and translate laboratory findings back into clinical applications." If the trial proves successful, it could accelerate vaccine development. Being in Singapore and having a model of collaboration has given their research a competitive advantage, Dr. Ooi said. "In Singapore, dengue is endemic and we have the expertise and technologies to tackle the problem."



Assoc Prof. Ooi Eng Eong

Added Dr. Ong, "Ultimately, the collaboration between both researchers and physicians accelerates the bench-to-bedside outcomes that benefits patients. There is nothing more powerful than to have patients treated by academic clinicians who are at the cutting-edge of clinical translational research."

Importantly, the Academic Medicine model creates a synergistic platform for clinicians, researchers and educators, said Prof. Rush. "From this interaction, you get academic products that improve medical care."

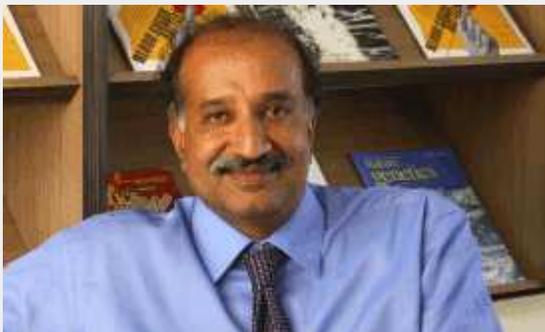
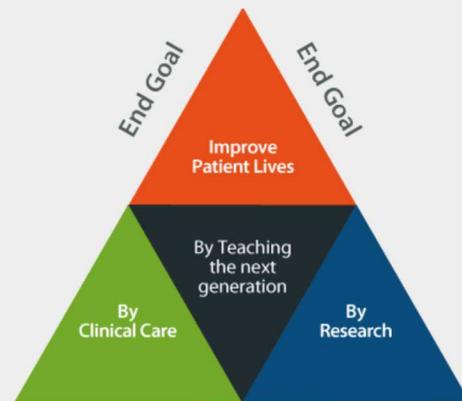
## In Brief:

### Academic Medicine is...

**"...academic medicine encompasses the traditional tripartite mission of educating the next generation of physicians and biomedical scientists, discovering causes of and cures for disease, and advancing knowledge of patient care while caring for patients."**

*- Academic Medicine, Journal of the Association of American Medical Colleges*

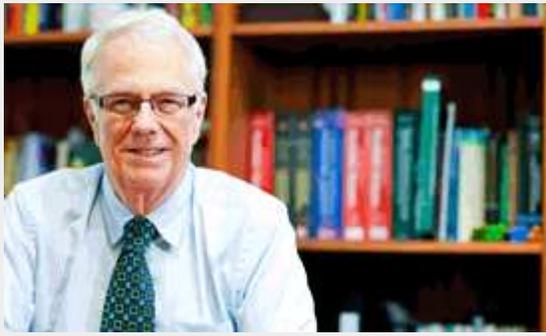
### Our vision for Academic Medicine



### On the partnership

**"The partnership is envisioned as an integrated working enterprise that guides and promotes the future of medicine, tapping on and combining the collective strengths of SingHealth's clinical expertise and Duke-NUS' biomedical sciences research and medical education capabilities."**

*- Prof. Ranga Krishnan, Dean*



### Clinical care +plus

"Merging clinical care, education and the development of new knowledge in academic medicine means medicine is taken beyond clinical care. Academic medicine means 'clinical care plus'. It means educating others to provide state-of-the-art personalized medicine (or medical care) and to develop new knowledge that improves the quality of care by challenging and changing conventional wisdom by finding better ways to screen, diagnose, and treat medical disorders."

*- Prof. John Rush, Vice Dean of Clinical Sciences*



### Role of Education

"There has always been great teachers in the Singapore public hospitals. Academic medicine provides additional incentives for faculty to become more skilled as a teacher. It also recognizes those that come up with ways to better educate our students through innovative curriculum or improved pedagogical approaches."

*- Prof. Bob K. Kamei, Vice Dean, Education*



### Role of Research

"Advances in medicine are driven both from discoveries made in basic science and from pursuing questions that first arise from a doctor's assessment of a patient. In an academic medicine environment, the researchers and medical practitioners working together in teams greatly accelerates the pace at which medically-important discoveries are made and actually applied for the benefit of the patient."

*- Prof. Patrick J. Casey, Senior Vice Dean, Research*

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## A year of discovery

*By Keith G. Emuang*

Since its inception in 2005, Duke-NUS has been offering a unique model of medical education. Aside from imparting relevant specialty knowledge, the goal has been to encourage its students to push the boundaries of medicine.

In nurturing a prowess in both science and medicine, this innovative approach is designed to deliver quality medical training anchored on developing a spirit of curiosity, inquiry, and self-directed learning.

The highlight of the four-year course is the research year (3rd year) when students are immersed in the realm of clinical, translational or services research that sees them working closely with an assigned clinical mentor - a formula that has already begun to reel in the accolades.

This year, two final year Duke-NUS students received prestigious awards for their 3rd Year research projects; one in ophthalmology and the other in neurology.

## Vision ahead

In April, Foo Li Lian was awarded the Young Investigator Award (YIA) at the 19th SGH Annual Scientific Meeting (ASM) for her research study on primary angle-closure glaucoma (PACG).

Attached to the Singapore National Eye Centre (SNEC) during her 3rd Year at Duke-NUS in 2010, Li Lian was involved in a 3000-sample population-based study to identify the determinants of angle width in Chinese Singaporeans.

She outlined, "My aim was to incorporate both new and established anatomical parameters in predicting angle width in order to allow us to gain a deeper understanding of the pathophysiology behind PACG."



*Foo Li Lian (left) and Prof. Aung Tin in conversation*

Professor Tin Aung, Senior Consultant and Head, Glaucoma Service, Singapore National Eye Centre, was Li Lian's mentor during her research year.

"Angle-closure glaucoma is a major cause of blindness in Singapore and is prominent in a large number of the Chinese population, especially the elderly. Hence, the significance of Li Lian's study was a major lead," stressed Prof. Aung.

He added, "She is mature and very motivated, had a good grasp of statistics and is a quick study. Also, her depth of knowledge, and competency and skills as a trainee doctor is most impressive."

What was particularly interesting was that her lack of any formal training in conducting research did not seem to dampen her drive. If anything, it spurred her to make full use of every learning opportunity she had with Prof. Aung and his team.

"The learning curve was steep but the whole team was patient and enthusiastic, and their strong passion had slowly rubbed off on me. Also, my mentor had heavily invested effort and time in teaching and guiding me along. He was a role model and an inspiring mentor," she said.

On a professional level, Li Lian was quick to point out how the experience has benefited her.

She acknowledged, "Thanks to the unique approach of Duke-NUS to dedicate a full year to conduct our investigations of interest, I have gained a whole new perspective and insight into the research of ophthalmology and its subspecialties. The research skills and ethics a student picks up during this time will definitely pave the way for a future as a budding clinician."

For future 3<sup>rd</sup> Year Duke-NUS students, Li Lian offered this piece of advice.

"The excellent, dedicated and inspirational mentorship and guidance is critical but you have to maximize and make full use of the opportunity. This year long experience could potentially have a tremendous value-adding impact in your entire medical career."

Speaking of the future, Li Lian is looking forward to tap on her new knowledge and skills to bring - according to her - 'ophthalmology research and clinical practice to a whole new level'.

## Beyond nerves

Yong Ming Hui won one of three 'Best Poster Presentation' awards at the 45th Singapore Malaysia Congress of Medicine held in July 2011. It was organized by the Academies of Medicine Singapore and Malaysia, in participation with the Hong Kong Academy of Medicine.

Her presentation was a novel case-control study that characterized and compared the burden of non-motor symptoms between two groups of patients with chronic neurologic disorders, Parkinson's disease (PD) and Hemifacial spasm, with healthy individuals.

"My mentor highlighted the non-motor symptoms in PD and other chronic neurological disorders that cause sleep and mood disturbances, and cognitive impairment, are not adequately identified and treated in clinical practice, and these can significantly reduce a patient's quality of life," she shared.

Dr. Tan Eng King, Associate Professor at Duke-NUS and Senior Consultant, Department of Neurology (NNI-Singapore General Hospital Campus), was Ming Hui's mentor. In turn, she was his shadow every other day for a year.

"She was an unusual student who was determined to see through the conceptualization, planning and execution of her study. With a relatively large base of 500 subjects, it was a very time-consuming process to undertake the clinical assessments of all of them," observed Dr. Tan.



*Yong Ming Hui with Professor Patrick Li, chief judge and President, Hong Kong College of Physicians at the Award ceremony on 23 July at the Marina Mandarin Hotel. Ming Hui received a Certificate of Achievement (Merit Prize) for her poster presentation.*

Tapping on Dr. Tan's deep clinical and research experience, Ming Hui was able to map out the best strategies to undertake a novel study that was both relevant and valid.



*Assoc Prof. Tan Eng King (left) and Yong Ming Hui in the wards*

"He was always willing to clarify my questions and doubts, and helped me refine the study's design and overcome difficulties I faced," revealed Ming Hui, who also attended numerous seminars, courses and discussions with other clinical research faculty members.

Invariably, this helped her to understand the critical elements required to construct a research hypothesis, conduct a proper research study, perform statistical analyses and ultimately, to submit a high quality presentation.

She revealed, "I now appreciate the need to be attentive to the problems that patients face in their daily lives, be vigilant in spotting clinical trends as well as look at various treatment strategies that can help them improve their quality of life."

Ming Hui had discovered how a passion for research and generating new knowledge can enhance one's experience in clinical practice. It was likely this passion that translated into her taking a merit prize for 'Best Poster Presentation', which was judged on scientific merit, presentation and novelty.

What surprised the judges most was the fact that she was a student in a competition of 40 submissions made mostly by doctors and specialists.

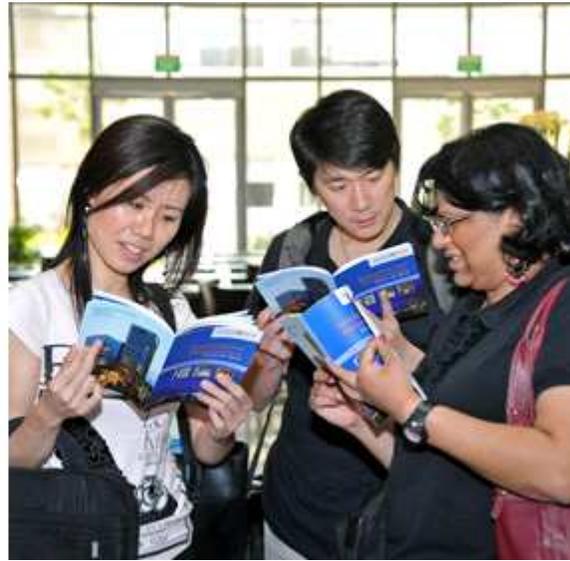
"All credit to her because she has the right attitude. She planted the seed and watered the plant for a year," commented Dr. Tan, who also indicated plans to use Ming Hui's research data as a springboard for other longitudinal studies.

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### **Related story:** MD Year 3 students' Research Presentation Day in slideshow



*Our annual Research Day on 24 Aug 2011 showcased research projects by our third-year MD students.*



*Our students explained their projects, sparking off some lively conversation between faculty, students and members of the general public.*



*Tertius Tuy, runner-up in the Clinical Science Category, presents his project to the audience at the Duke-NUS auditorium.*



*(Left) Dean Ranga presents the prize to Guadalupe, runner-up in the Basic Science Category. (Right) Winners all! Congratulations to prize winners of the Basic Science Category and the Clinical Science Category. From left, Ignasius Jappar, Tertius Tay, Yong Ming Hui, Guadalupe, Melinda Tan and Esther Chang.*

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## Paying it forward

For Dr. Karen Nadua, her contribution to the 2011 Class Gift Fund was more than a mere donation. It was a token of appreciation for being able to fulfill her dreams. "From the school, I garnered not only a medical degree, but also invaluable gifts like mentorship from the faculty, friendships with classmates and schoolmates and treasured memories these past four years," she shared.

The Class of 2011 set a laudable precedent with a 100 per cent participation rate as Duke-NUS' pioneer graduating class. This despite not having even embarked on their medical careers and having personal financial obligations.

Commenting on the full participation of the Class of 2011, Dean Ranga Krishnan said, "I know that the hearts of our alumni are with us as they contribute directly to the growth of Duke-NUS and helping the medical students who follow behind them."

Parents and students gave generously, raising an excellent total of S\$64,778, which is exemplary considering that the first class comprised less than 30 students. Additional contributions from Duke-NUS' education faculty and a Duke-NUS Governing Board member rounded up total contributions to S\$100,000.

Said an anonymous faculty member who matched the students' donations to the 2011 Class Gift Fund, "I believe in creating opportunities for students to live up to their fullest potential in the hope they will contribute back to society and am glad to support this initiative."

For some, contributing to the class gift was a way of paying it forward. Duke-NUS admits students on merit, without regard to their financial backgrounds. The Class Gift Fund goes towards supporting student bursaries, student community projects or defraying conference expenses.

Dr. Lim Miao Shan benefitted from Duke-NUS donors' generosity when she pursued her medical training.



*(From left) Dr. Lim Miao Shan, Assoc Prof. Tan Chee Kiat and Dr. Karen Nadua. Assoc Prof. Tan tutored both Drs. Lim and Nadua in Internal Medicine in their 2nd and 4th years and often shares and emphasizes on giving back.*



**"From the school, I garnered not only a medical degree, but also invaluable gifts like mentorship from the faculty, friendships with classmates and schoolmates and treasured memories these past four years."**

*– Dr. Karen Nadua (center, flanked by family & friends)*

"I had received financial aid from Duke-NUS throughout the course of my studies," she shared. "It enabled me to focus my time and energy more towards learning and greatly alleviated my family's financial burden. Thus, it is in the spirit of paying it forward that my fellow students decided that we should all participate in the Class Gift."

The Class of 2011 understood the importance and benefits of the Class Gift and needed little encouragement to give generously. They even contributed the proceeds raised from snacks and beverages sold at the students' lounge. Said Miao Shan, "Everyone naturally felt that it is only right that we contribute (in whatever small ways we could) towards our school which had given us much financial support throughout the course of our study."

Karen agreed, noting that donating was a gesture of solidarity. "For the pioneer class, the school is especially close to our heart. I believe we also wanted to make a statement about our commitment as a class to the school's future even after we have graduated."

Added Miao Shan, "Duke-NUS is what it is today partly because of generous donations and sponsorships from various organizations and donors. We are grateful towards them and would like to emulate this spirit of giving. There is a Chinese saying that reminds us not forget our roots and keep in mind the spirit of giving back to others – whether in monetary contributions or time to teach others."

## Giving to Duke-NUS

Donors play a significant role in ensuring that our medical students receive the precious gift of education. Giving supports our aspiring clinicians and clinician-scientists in these aspects:

**Community Outreach** – Your gift helps students participate in both local and regional community projects and allows them to develop servant leadership skills.

**Medical Education** – Your gift provides financial assistance for students to attend and present at symposiums that are essential to their learning and development.

**Student Aid** – Your gift will help alleviate the financial burden of needy students through bursaries.

Please contact [development@duke-nus.edu.sg](mailto:development@duke-nus.edu.sg) or **Tel: +65 6516 8682** to make this happen or to find out more about giving to Duke-NUS.

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## The class of 2015 begins their medical journey



This year's White Coat ceremony for the fifth intake of students (Class of 2015) was held on 12 August 2011 in the College of Medicine Building Auditorium. The donning of a white coat - a symbol of becoming a member of the medical community committed to clinical service and patient care, is the culmination of the Foundations Course. The Foundations Course emphasizes humanistic values, a selfless commitment of students to medicine as a calling or vocation, and the importance of working collaboratively with others for the benefit of patients and the profession. As they stood together reciting the modern Hippocratic Oath, the students humbly dedicated themselves to the practice of medicine. Dr. Jean Spaulding, trustee of the Duke Endowment and consultant to Duke Medical Center and the Duke University Health System, administered the Hippocratic Oath.

Present for the ceremony were many parents and other relatives, as well as the guest of honor Mrs. Tan Ching Yee, Permanent Secretary (Education), and many Duke-NUS faculty and Governing Board members. The latest class adds to the rich diversity and backgrounds of the Duke-NUS family. It brings the total student population to over 240 students. Over half of them are Singaporeans and Singapore Permanent Residents, and the rest hail from 11 different countries, including Russia and Australia, a first for the school.

One student who joined Duke-NUS after doing her Master's in Biomedical Engineering at Duke in the U.S is Choo Min. "I had set my mind on entering Duke-NUS during my third year of undergraduate study at NUS, even before I had applied to Duke University to do a Master's in Biomedical Engineering which I completed in 2010. It is very fortunate that I have access to such

an education in my home country and can be trained in the local hospitals. Singapore is where I intend to stay, where I can support and contribute to healthcare locally and regionally."

Another student, Alfonso Tan shared, "The ability to make a difference in someone else's life through medicine was central in my decision to join the school. Medicine and research are intrinsically linked and advancements in clinical practice can only occur through constant experimentation. The MD/PhD training (a track in the third year) will prepare me well for such a career."



"I love the fact that everyone has at least a Bachelor's degree. It shows the amount of passion and dedication that they have in choosing to enter Duke-NUS, especially in the context of Asia, where medicine is usually an undergraduate degree. We would have become a professional in our own fields following graduation, but here we are pursuing medicine with passion."

- Choo Min, MS1



"Duke-NUS ranked among my top choices of schools for post-graduate education. In the four years since its establishment, Duke-NUS has expanded tremendously - recruiting both faculty and students of good caliber."

- Alfonso Tan, MS1

Applications for the Class of 2016 are now open. Check out [InsideDukeNUS](#) to see the student conversations on why they have chosen to study at Duke-NUS.

## MD year 1 foundations course activities



*Orientation program organized by Year Two seniors with exciting icebreakers and teambuilding activities.*



*(Left) Year One students share a meal together in a food center and (right) complete the Outram campus edition of "The Amazing Race".*



*(Left) Prof. Bob Kamei, Vice Dean of Education in basketball gear surprising the class in his annual welcome address. (Right) Students and faculty having a hearty laugh during the group photography session.*



*The Duke Corporate Education Workshop imparts knowledge and tools on working effectively in teams and managing conflict and diversity.*



*(Left) Prof Tan Ser Kiat, Group CEO of SingHealth, in conversation with our Year One students. (Right) Bonding over a bonfire. Senior students hosted a BBQ for our Year One students.*



*(Left) Assoc Prof. Craig Stenberg, Associate Dean for Student Affairs & Admissions presents NUS president Prof. Tan Chorh Chuan a token of appreciation, while Dr. Jean Spaulding, a Duke Endowment trustee looks on. (Right) An inspiring talk by Dr. William Tan, the first man to complete the North Pole Marathon on a wheelchair.*



*(Left) The donning of a white coat - a symbol of commitment to clinical service and patient care during the White Coat Ceremony. (Right) Our Year One students recite the modern Hippocratic Oath.*

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## The music of medicine

Music has been found to have a positive, uplifting effect on human emotion. As such, music is often used to treat and comfort patients as a form of therapy. Duke-NUS students have done likewise by bringing joy and laughter to patients through the magic of music during the festive seasons at hospitals and hospices. A good number of our students engage in musical performances for the community throughout the year.

In this issue, Vital Science speaks to our resident student band, Acoustic Bop -- comprising Josh Chua, Giselle Reinoso, Apurva Thanju and Esther Low - on the harmonious twinning of Medicine and Music.



*(From left) Esther Low, Apurva Thanju, Josh Chua and Giselle Reinoso from our resident student band, Acoustic Bop.*

### How did music and medicine meet for you?

**Josh:** Medicine and Music first came together for me when I worked with Dr. Kenneth Lyen, a pediatrician and a composer. We brought together three musicals including one that had a second run at the Raffles Hotel. One of the many reasons I wanted to be a physician is to be someone who is empathetic towards others. There is a commonality in healing and music -- the Greek God, Apollo, was both the God of medicine and music.

**Apurva:** In the purest sense, both are about humanity: one is about the expression of our identity and the other is the process of healing the physical manifestation of that identity. Music and medicine require intense practice and discipline, and the challenge in both is to turn beautiful theory into useful practical elements.

**Esther:** Music and medicine are indeed very different, the former being traditionally considered an art and the latter, a science. I suppose the common ground is passion. I usually sing A Cappella, and being part of a band has taught me about synergizing instruments and voices. Our band members are so diverse in our backgrounds, but I love the synergy we have created. In medicine, there is the same approach -- many different factors have to be in place and a healthcare team has to collaborate to heal a patient. Music and medicine allow for a colorful mix of individualities within a team. On a personal note, singing is therapeutic and allows me to unwind when medical school gets too crazy.

**Giselle:** I grew up in the Philippines and remember when nuns would come by my grandmother's house. They'd sing enthusiastically, and I'd dance in the center of their little circle without a care

in the world. To make music, all you need is enthusiasm and a lot of heart. And isn't that what doctors have? While music and medicine are theoretically very different, they are complementary. No one said I couldn't be a singing doctor. Singing has trained me to learn songs and lyrics very quickly and this helps when I have to learn massive amounts of information; when you turn the information into a song or a dance, you will never forget it!



**“Every member has to come prepared. Only when each of us does our homework beforehand, does the time spent together as a band or a team be enjoyable, synergistic, and fruitful.”**

*– Esther Low, on the similarities between studying medicine and playing music*

### **The band has been supporting many Duke-NUS events. How did you first come together as a band?**

**Josh:** In the beginning of the year, our class put on an item for an inter-faculty talent competition. We found a trove of musical talent within a small class and did a Singaporean parody of “California Girls”. I created the skeleton track on which musicians, singers and a rapper layered on during the performance. The collaborative effort was very similar to our TeamLEAD process where team members contribute information and opinions to help develop the answers. I guess, our educational approach has sneaked its way into how we organize our music groups.

### **In what other ways does making music mirror the way you learn at Duke-NUS with TeamLEAD?**

**Giselle:** Each member of the band has a different background and different set of skills, similar to a team composed of biologists, chemists, engineers and neuroscientists. This makes for very interesting discussions because each person's approach to answering a question is different, not unlike each person's unique interpretation of a song. Although we don't always come to an agreement, the experience of solving and creating something together is why we enjoy what we do.

**Josh:** Although a musical performance may seem effortless, there are a lot of decision processes and problem solving. Understanding musical theory and having the mental dexterity to appreciate permutations of the rules come together to produce original works. This reminds me of medical science. While working on a stem cell project, I had a series of frustrating failed experiments. However, via a permutation of two methods I had an “eureka” moment – just like when I manage to find the best match of notes and



**“Facilitating and cultivating dialog for learning and exploring possibilities is really what TeamLEAD is about.”**

*– Apurva Thanju, on TeamLEAD*

chords in a melody.

**Esther:** Every member has to come prepared. Only when each of us does our homework beforehand, does the time spent together as a band or a team become enjoyable, synergistic, and fruitful.

**Apurva:** When we get together to perform a song, we have only a rudimentary idea of how a certain song will sound. But our different talents and styles have created a certain flair as we play off of each other's ideas and talents. There is often a lot of room for discussions, for rhythm, for harmonies. I remember Giselle, Esther and I once sang O Holy Night for our Christmas concert. After much discussion and practice (and voice lessons for me from them both!) we managed to create something that was unique. I think it's true in medicine too. There is so much value in discussion because the whole is always so much more than the sum of the parts. This is very important to medicine in general and Duke-NUS in particular, because facilitating and cultivating dialog for the sake of learning and exploring possibilities is really what TeamLEAD is about.

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## NEWS IN BRIEF

- ▶ President Brodhead meets Duke alumni in Singapore
- ▶ Minister of Health and Minister of State visit Duke-NUS
- ▶ Duke-NUS and YLLSoM students work together
- ▶ Lien Center for Palliative Care appoints Research and Education directors
- ▶ PhD program gains traction
- ▶ Duke-NUS education team shares team-based learning approaches in Cambodia
- ▶ Benjamin Sheares Professorship recipient meets donors

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*President Richard H. Brodhead (right) and Dr. Mike Merson (left) addressing the audience.*

## President Brodhead meets Duke alumni in Singapore

On 5 July 2011, Duke University President Richard H. Brodhead visited Singapore as a part of The Duke Idea, a series of talks on how Duke is harnessing its strengths to improve health around the world.

Almost 100 Duke students, alumni and their families residing in Singapore attended the event. Dr. Mike Merson, interim vice president and vice provost for Global Strategy and Programs, was also present to share his thoughts and vision.

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## Minister of Health and Minister of State visit Duke-NUS

Minister for Health, Mr. Gan Kim Yong and Minister of State, Dr. Amy Khor visited Duke-NUS on 30 June 2011. They were greeted by key representatives of Duke-NUS and also Prof. Tan Ser Kiat, Chairman, Development Committee and Group CEO of SingHealth.

Prof. Tan kick-started the program by giving an

*(From left) Ms. Giselia Giam, Prof. Patrick Casey, Prof. Bob Kamei, Minister Gan Kim Yong, Prof. Tan Ser Kiat, Dr. Amy Khor, Dr. Lau Hong Choon, Assoc Prof. Tan Say Beng and Mr. Christopher Koh.*



*Prof. Shirish Shenolikar briefs Minister Gan Kim Yong during the tour of the Cancer & Stem Cell Research Laboratory.*

overview of Duke-NUS' partnership with SingHealth in education and research. The ministers were given presentations on the research programs, as well as its unique teaching methodology - TeamLEAD. As part of the visit, the ministers also toured the campus, research laboratories and the educational facilities.

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*Guests at Wine and Dine 2011 (Photo credit: Pinhong)*

*Front row (from L-R): Mr. Tony Chew, Duke-NUS Governing Board Chairman, Assoc Prof. Marie Clemont, Prof. Bob Kamei and Ong Wen Chong*

*Back row (from L-R): Prof. Arthur Lim, Mr. Andy Ng, Assoc Prof. Lau Tang Ching, Dr. Craig Stenberg and Mayannak Dalakoti and Dean Ranga Krisnan*



*Students from Duke-NUS and YLLSoM entertaining the audience with their rendition of popular classics. (Photo credit: Pinhong)*

## Duke-NUS and YLLSoM students work together

Duke-NUS students and Yong Loo Lin School of Medicine (YLLSoM) students joined hands to serve a greater cause and for some witty repartee, as they worked together to strengthen and foster exchange and friendships within the medical student community.

### Wine & Dine 2011

It was an evening of glitz and glamour with a purpose. Students from both Duke-NUS and YLLSoM organized a gala event, Wine & Dine 2011, where proceeds will benefit student bursaries in both schools.

Almost 200 people enjoyed dinner at the event held on 17 September, in the beautiful grand colonial setting of the Goodwood Park Hotel. The guests were serenaded by a string quartet and sipped cocktails at the reception. Wines were auctioned under the rap of a hammer. Guests were also enthralled by several musical performances that were also up for bidding.

Said Foo Li Lian on her experience in working with fellow students from YLLSoM, "As fellow medical students, we understand and help each other in our medical journey. I hope that the success of this joint effort will inspire our juniors to continue this proud tradition of looking out for those in need and strengthening the bond within the medical community."



*Duke-NUS MS1 student Ivan Ogloblin on the proposition team makes his point. (Photo credit: SMA)*

Chuan.

The debate topic was a delicate and tricky one - "Are women better off making lives than saving lives?" The mixed debate teams comprised students from both schools. Representing Duke-NUS were Ivan Ogloblin (proposition) and David Tainter and Clarissa Tio (opposition).

On his interactions with students from YLLSoM, Kenneth Goh, a Duke-NUS MS3 student said, "It's always fun to work with our friends from YLLSoM. The work we do together is meaningful and they always bring with them an infectious amount of enthusiasm!"

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*(From left) Dr. Angelique Chan, Dr. Jeremy Lim, Centre Executive Director and Dr. Noreen Chan*

## **Lien Center for Palliative Care appoints Research and Education directors**

The Lien Center for Palliative Care is Asia's first center for palliative care education and research. To strengthen and drive its initiatives, the Center has appointed Assoc Prof. Angelique Chan as Research Director and Dr. Noreen Chan as Education Director.

Assoc Prof. Angelique Chan will be developing workshops, conferences and bring in experts to build up capacity in palliative care research. She is also overseeing the establishment of the Lien Center for Palliative Care grant call for clinician-initiated research. In addition, she is actively involved in developing a national palliative care strategy for Singapore.

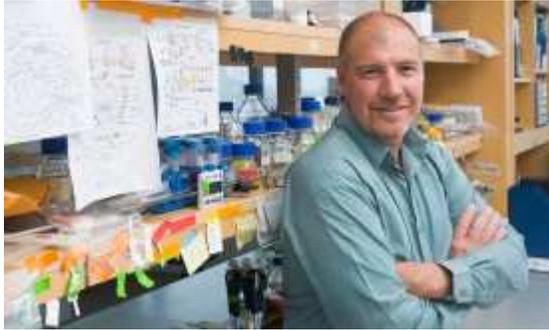
Dr. Chan is a faculty member in Sociology at the National University of Singapore. Over the past 15 years, she has collaborated extensively as Principal Investigator or Co-Investigator with researchers in Japan, the Philippines, Taiwan, Thailand, Indonesia and the United States on studies on health, living arrangements, economic security and the intergenerational transfers of older adults in Asia. She is also the Director of the Tsao Foundation Research Initiative on Aging.

As Education Director at Lien Center, Dr. Noreen Chan plans to work with industry partners to produce innovative courses, workshops and symposia. These education platforms are designed not only to strengthen the skills and capabilities of healthcare workers and doctors who specialize

in palliative care, but also to educate all who encounter the issue of death and dying as part of their work.

Dr. Chan is a Senior Consultant in the Department of Hematology-Oncology at the National University Cancer Institute, Singapore and a visiting consultant to Dover Park Hospice. She is also a member of the Subspecialty Training Committee for Palliative Medicine and the Honorary Treasurer of the Pain Association of Singapore.

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*Assoc Prof. Scott Summers*



*Dong Di, PhD class of 2010*

## PhD program gains traction

Duke-NUS recently completed its second intake of students in the Integrated Biology and Medicine (IBM) PhD program. The program equips researchers with the skills and knowledge to take their research findings from "the bench to the bedside".

In the first year of the PhD program, students undertake a 15-week core course, "Molecules to Medicine". They focus on basic science, clinical research and translational research concepts conducted using a team-based learning approach. The core course is complemented by two 8-week lab rotations of the student's choice.

On the team-based approach, Assoc Prof. Professor Scott Summers, Director of Graduate Studies said, "The approach levels the playing field such that student and faculty become equally engaged in the discussion and process. Rather than using a top-down mindset, students are encouraged to challenge content experts."

Assoc Prof. Eric Finkelstein, Deputy Director in the Health Services & Systems Research program, agrees that the team-based approach works well for students as they start to pursue cross-cutting research interests in their second year. Dr. Finkelstein mentors Dong Di, a PhD student from the pioneer class of 2010.

He said, "As I was teaching Dong Di how to do cost-effectiveness analysis for her project, she was also sharing with me knowledge on genetics and biology."

Prior to pursuing her PhD, Dong Di took her Bachelors in Biological Sciences at NUS. She shared, "The curriculum allowed me to leverage on my knowledge in biomedical sciences to develop the expertise in the broad skills required to drive translational medical research."

To find out more about the PhD in IBM, watch this: [Open Conversations Video with Scott Summers.](#)

Applications for the next PhD in IBM program closes early next year. To find out more, visit: [www.duke-nus.edu.sg/web/education/phd-program](http://www.duke-nus.edu.sg/web/education/phd-program).

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*Participants in discussion, led by our education faculty.*

## Duke-NUS education team shares team-based learning approaches in Cambodia

Our education faculty conducted four workshops in Phnom Penh, Cambodia between 21-22 July 2011.

Prof. Bob Kamei, Vice Dean of Education and Assoc Prof. Sandy Cook, Senior Associate Dean, Curriculum Development, were there to train more than 40 educational leaders and staff from a hospital's Continuing Medical Education and

MCAT departments.

The participants had the opportunity to experience team-based learning as an instructional methodology. Participants appreciated the dynamics of transforming groups into a cohesive team. Prof. Kamei and Assoc Prof. Cook also coached a group of facilitators on how to develop and deliver a teambuilding workshop in Cambodia.

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*Mrs.Boon-Ngee Sebastian receives the Duke stone from SingHealth Group CEO, Prof. Tan Ser Kiat, while Dr. Joseph Sheares looks on.*

## Benjamin Sheares Professorship recipient meets donors

"My family is deeply touched by this honor bestowed on our late father." These simple words succinctly conveyed the sincerity of the Sheares family, represented by Dr. Joseph Sheares at a dinner, held on 11 July 2011 to thank donors of the Benjamin Sheares Professorship in Academic Medicine. The endowed Benjamin Sheares Professorship in Academic Medicine is established by Duke-NUS with a combined S\$2.5 million gift from Tote Board and SingHealth Foundation as well as a significant donation from the Sheares family. This is the first professorship to be named in honor of a founding father of Singapore medicine and Singapore's second President.



*Prof. Soo (right) receives the professorship plaque from Dr. Joseph Sheares (left) on 28 May 2011, during Duke-NUS's first pre-graduation celebration and hooding ceremony.*

Professor Soo Khee Chee, inaugural recipient of the Benjamin Sheares Professorship, was present to meet the donors and personally outline his plans to fulfil the expectations of this award and serve the community. Prof. Soo Khee Chee is the founding Director of the National Cancer Centre Singapore and Deputy Chief Executive Officer of Singapore Health Services, and the Vice Dean for Clinical and Faculty Affairs at

Duke-NUS.

Said Prof. Soo, "I am personally inspired by the legacy of the late Dr. Benjamin Sheares and am honored and humbled to be conferred this professorship. Teaching and mentoring medical students constantly energizes me and enables me to witness their growth. Their vigor, thirst for learning and inquiring minds are constant reminders for me to stay curious, innovate and improve on the practice of medicine."

Mrs. Boon-Ngee Sebastian, Tote Board's Director for Grant Management and SingHealth Foundation's Executive Director Dr. Kwa Chong Teck each received a memento of a Duke stone in appreciation for helping to set up the Sheares Professorship.

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## RESEARCH NEWS

- ▶ Unveiling the 'molecular face' of gastric cancer for personalized cancer treatment
- ▶ w'RAC'k the cancer cells by triggering self-eating
- ▶ Novel brain tumor suppressor gene discovered
- ▶ Study offers clues into the mechanism of mutation of influenza viruses
- ▶ Identifying the complexities in dementia care

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Assoc Prof. Patrick Tan

## Unveiling the 'molecular face' of gastric cancer for personalized cancer treatment

Associate Professor Patrick Tan, from the Program in Cancer and Stem Cell Biology at Duke-NUS, has distinguished the genetic differences in two types of gastric cancer, a move that paves the way for customized cancer treatment that can boost the effectiveness of chemotherapy, while minimizing the side effects.

Compared to visual diagnosis via a microscope to determine if stomach cancer has intestinal or diffuse characteristics, Dr. Tan has utilized genechips to map the DNA of tumors. "This has allowed us to see the molecular face of gastric cancer and classify tumors," he said. "Different cancers react differently to different chemotherapy drugs. By establishing the signature of a cancer, we can identify which drugs are most effective." For instance, the chemotherapy drug Fluorouracil is effective 55 per cent of the time against intestinal gastric tumors, but only effective in 23 per cent of the time when used to treat diffuse tumors. Knowing which type of cancer is present can better guide doctors to select more effective drugs.

These findings – published in the journal *Gastroenterology* in August – are being used in a clinical trial run by the Singapore Gastric Cancer Consortium (SGCC). The SGCC comprises a multi-disciplinary group of scientists and clinicians, from the National University Health System, Duke-NUS Graduate Medical School, National University Cancer Institute, Singapore, National Cancer Centre Singapore, Cancer Science Institute, Singapore, the Genome Institute Singapore and four public hospitals.

The study will profile gastric tumors and roll out treatment based on the genomic signature of each cancer. Instead of the conventional three-drug chemotherapy regime, clinicians will use a two-drug treatment regime that aims to be more effective, less toxic and less expensive. The trial is a joint effort by the National University Cancer Institute, Singapore (NCIS) and the National Cancer Centre Singapore (NCCS).

In Singapore, gastric cancer is often diagnosed in advanced stage of the disease. It kills 330 Singaporeans each year and is the fifth most common cancer in males and seventh in females. In 2007, a S\$25 million dollar translational clinical research grant was awarded to the SGCC to tackle gastric cancer.

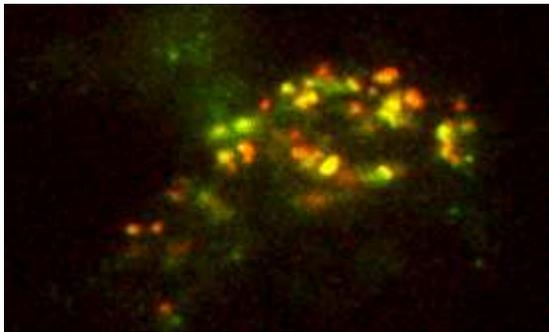


*Asst Prof. Mei Wang*

## w'RAC'k the cancer cells by triggering self-eating

One of the greatest challenges in cancer treatment is reducing the toxicity of the cancer drugs by attacking processes specific to cancer cells. A new discovery by Asst Prof. Mei Wang, Program in Cancer Stem Cell Biology at Duke-NUS, brings some progress to the search for more targeted forms of cancer treatment with her work on identifying specific proteins involved in the process of "self-eating" in cancer cells.

Cancer develops because their cells have faulty genes. The proteins made from these genes either activate certain processes too much, or suppress other process excessively. The results are uncontrolled growth, resistance to therapy-induced cancer cell death, and tendency to spread to other places. One of the most prevalent of these faulty genes found activated in over half of all human cancers is known as Ras. Dr. Wang's study has identified a Ras family member called Rac3 which, when disabled, enhances a kind of cancer cell death called autophagic (or self-eating) cell death.



*"Self-eating" in cancer cells*

These findings were published on line in the August issue of *JBC* (18 August 2011, doi:10.1074/jbc.M111.280990). "The identification of the role Rac3 plays in manipulating autophagy has opened up new avenues for drug development", said Dr. Wang. "We have been studying the therapeutic potential for inhibiting a process that mammalian cells used to decorate their protein by adding a lipid tail to the protein. For many of these proteins, if the lipid is not added on correctly, the function of the protein can be fundamentally compromised. The Ras family of oncoproteins, including the aforementioned Rac3, are modified this way."

Dr. Wang and her team found that blocking this process – called prenylation – can increase the rate of cancer cell "self-eating" leading to their demise, likely through inhibiting Rac3 function. "One of the greatest challenges of developing cancer therapy is to identify cancer-specific proteins or cancer-specific processes so that they can be attacked directly, thereby sparing normal cells," said Dr. Wang. "Therefore, there is potential in targeting Rac3 in specific cancer cells which has suppressed intrinsic autophagy. Duke-NUS has filed a patent on this discovery which indicates that agents that selectively inhibit Rac3 function may slow the growth of cancer, either on their own or in combination with other anti-cancer drugs.



*Asst Prof. Wang Hongyan*

## Novel brain tumor suppressor gene discovered

A faculty member in the Neuroscience and Behavioral Disorders Program of Duke-NUS is a senior author of a paper just published in the prestigious journal *Developmental Cell* (13 September 2011).

Asst Prof. Wang Hongyan and her team have shed light on a hitherto-unrecognized process that is related to how brain tumors form.

The team discovered a novel brain tumor suppressor gene termed Ana2 (anastral spindle 2) in *Drosophila*. The team further found that the suppressor gene is linked to another brain tumor suppressor with the unusual name of Mud by a specific motor protein. The two suppressors interact with each other and function in the same pathway to suppress tumor formation.

The same study showed that Ana2 is critical for the asymmetric division of neural stem cells, by which the balance of neural stem cell self-renewal and differentiation is achieved. Discovering the pathway and determining how it functions in brain development is important for understanding the mechanisms underlying brain tumor development, and could provide a new avenue to developing therapies for brain and related tumors.

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*(From left) Co-authors Dr. Gavin James Smith and Dr. Vijaykrishna Dhanasekaran*

## Study offers clues into the mechanism of mutation of influenza viruses

In the longest study of its kind, Duke-NUS researchers have discovered that the transportation of live pigs across geographical boundaries have caused swine flu viruses to mix with local viruses and form new strains. This has increased the diversity of swine influenza viruses and adds to the challenge of finding vaccines for each newly mutated version.

To gain more insight into the mechanism of influenza virus evolution, researchers studied the epidemiology, genetics, and antigenic properties of more than 650 samples of swine flu viruses, 800 blood samples garnered across 12 years and 34 years' worth of data on swine flu viruses. Said lead researcher Vijaykrishna Dhanasekaran, Assistant Professor at Duke-NUS' Laboratory of Virus Evolution, "It is important to monitor viruses in swine, especially those that can emerge in humans that we do not have antibodies for." Dr. Vijaykrishna is a faculty member of the Duke-NUS Program in Emerging Infectious Diseases. The study, which was published online in *Nature* in May, also found that two common H1 subtype viruses and the human H3N2 viruses were frequently detected in swine. Several combinations of these three lineages were also detected in pigs, including some avian (bird) viruses.

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(From left) Prof. David Matchar, Amina M. Islam and Dr. James Thompson

## Identifying the complexities in dementia care

To understand the identify issues and challenges associated with cognitive impairment (CI)/dementia, a team of Duke-NUS researchers garnered perspectives from stakeholders that dealt with dementia. This comes the burden of dementia incidence rises in tandem with the ageing population in Singapore, a trend that has far-reaching impact on not only the country's healthcare system but carries socio-economic effect as well.

Though a series of in-depth interviews, researchers found that caring for dementia is a complex and multi-faceted issue that involves not only the broader healthcare system (such as hospitals or step-down care institutions) but family/social dynamics, education, living arrangements, financial considerations and even mindsets and attitudes. "The results support the notion that this is a condition with causes and effects well beyond the biological, with crucial social, financial, and organizational elements," noted Amina M. Islam, one of the study's authors. These findings point to the need for an integrative analytic approach such as system dynamics that takes all these perspectives into account, she added.

In the study, stakeholders interviewed also raised the need for more policy analysis, further research, and service innovation and evaluation. This leaves scope for more awareness campaigns, medical subsidies or financial help, enhanced integration of care, training for healthcare workers involved in dementia care, strengthened community as well as family and social support. "More broadly, many comments highlighted the importance of coordination among stakeholder groups, such as practitioners, researchers, and policy-makers, as a strategy for promoting system improvement," said Prof. David Matchar, Director of Health Services and Systems Research, Duke-NUS.

The study – which was supported through the STaR award by the Singapore National Medical Research Council – was published in *International Psychogeriatrics* in June 2011.

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GRANTS AWARDED

- ▶ Regulation of Circadian Rhythms
- ▶ Modulation of thyroid hormone action by SIRT1 histone deacetylase activity
- ▶ Marrying microRNAs and microfluidics to spawn new insights in CNS axon regeneration
- ▶ The role of eukaryotic initiation factor 2 alpha phosphorylation
- ▶ Immune pathology during Dengue Virus Infection
- ▶ Dissecting the Role of the Polupromidine Tract Binding Protein in Dengue Virus Replication

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Here are the details of projects awarded to Duke-NUS researchers in NMRC Nov 2010 Grant Call.

No.	PI	Dept	Project Title (Please click titles for details)	Grant Call	Duration (Months)
1.	David Virshup	CSCB	Regulation of Circadian Rhythms	NMRC Nov10 Grant Call	36
2.	Paul Yen	CVMD	Modulation of thyroid hormone action by SIRT1 histone deacetylase activity	NMRC Nov10 Grant Call	24
3.	Marc Fivaz	NBD	Marrying microRNAs and microfluidics to spawn new insights in CNS axon regeneration	NMRC Nov10 Grant Call	24
4.	Hyunsoo Shawn Je	NBD	The role of eukaryotic initiation factor 2 alpha phosphorylation in amyloid-beta induced dendritic spine loss	NMRC Nov10 Grant Call	24
5.	Ashley Lauren St. John	EID	Immune pathology during Dengue Virus Infection	NMRC Nov10 Grant Call	24
6.	Azlinda Binte Anwar	EID	Dissecting the Role of the Polupromidine Tract Binding Protein in Dengue Virus Replication: A Possible Target for Small Molecule Intervention	NMRC Nov10 Grant Call	24

**Total Amount of Funding Received : S\$1,963,234**

## Synopsis

### 1. Regulation of Circadian Rhythms

David Virshup, Cancer and Stem Cell Biology

Circadian rhythms refer to the 24-hour biologic clock that operates within our body, controlling activities like sleep-awake cycles, wakefulness and metabolism. Disruption of circadian rhythms by jet-lag and shift work causes real biological stress, leading to serious diseases like cancer, diabetes, sleep disorders and depression. Circadian rhythms are controlled by a group of proteins that oscillate every day, and mutations of these proteins result in rhythms change, which will subsequently lead to significant physiological consequences. Our project focuses on a key protein, Per2, that regulates the clock and oscillates during the rhythm cycle. A process known as phosphorylation, in which phosphate groups are added to the protein at specific sites, controls Per2 during circadian rhythms. Dr. Virshup's lab can measure subtle changes in rhythms of cultured mammalian cells, and will manipulate Per2 function and phosphorylation by various biological means to better understand the effects on circadian rhythms. Their study will help our understanding of sleep-wake cycles, with the hope this will help us understand how to alleviate circadian stresses, which will in turn provide important benefits to improve human health.

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### 2. Modulation of thyroid hormone action by SIRT1 histone deacetylase activity

Paul Yen, Cardiovascular and Metabolic Disorders

Thyroid hormones (THs) are important for the function of virtually all tissues throughout life. Thyroid hormone receptors (TRs) bind both TH and DNA located in the control regions of genes (response elements) regulated by TH. TH binding to TR and its binding to DNA causes chemical modifications of the chromatin proteins which surround DNA control regions of target genes. These modifications lead to changes in the shape of the chromatin that result in an increase the production of RNA (transcription) and protein products. SIRT1 is an enzyme which removes carbon (acetyl) groups from chromatin and its activity likely affects transcription. Interestingly, SIRT1 also is important for increasing lifespan as well as enhancing the metabolism of sugars and fats.

Our studies aim to show how SIRT1 causes chromatin changes that affect transcription of important liver genes regulated by TH and are involved in metabolism and aging using cell culture and mouse models. These studies also will demonstrate how TH regulation of gene transcription may change during different metabolic states such as fasting and overfeeding as well as aging. Our findings potentially could lead to new treatments to activate SIRT1, and thereby decrease the severity of metabolic diseases associated with obesity and aging.

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### 3. Marrying microRNAs and microfluidics to spawn new insights in CNS axon regeneration

Marc Fivaz, Neuroscience and Behavioral Disorders

One major reason for the devastating and permanent disabilities after spinal cord lesions and other types of central nervous system (CNS) injuries is the failure of CNS axons to regenerate. The genetic factors underlying the poor regenerative growth of CNS neurons are the focus of intense research and represent potential therapeutic targets for regenerative medicine.

MicroRNAs (miRNAs) are short non-coding RNA molecules that function as posttranscriptional regulators of gene expression. A few thousands miRNAs are estimated to modulate expression of

up to one third of all human genes, including those expressed in the brain. Changes in miRNA expression have been associated with global modifications of gene expression patterns during neuronal development and aging. We speculate that global miRNA-dependent changes in gene expression contribute to the poor regeneration capacity of adult CNS neurons. Our hypothesis predicts that manipulation of miRNAs levels may lead to the reactivation of an axon growth program following injury and promote CNS axon regeneration.

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#### **4. The role of eukaryotic initiation factor 2 alpha phosphorylation in amyloid-beta induced dendritic spine loss**

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

Alzheimer's disease (AD) is an incurable, degenerative, and terminal disease that affects more than 26 million people worldwide. The number of synaptic connections between neurons are progressively reduced in the brain of human AD patients, primarily due to amyloid beta (A $\beta$ ). However, no one understands how A $\beta$  causes synapse loss until now. Recent findings reveal that the level of the phosphorylated form of one protein, eIF2 alpha, is specifically increased and sustained in neurons exposed to A $\beta$  and also in the brain of human AD patients. Because eIF2 phosphorylation blocks the synthesis of new proteins essential for cell function, we propose that the increased and sustained phosphorylation of eIF2 alpha by A $\beta$  is responsible for synapse loss shown in human AD patients.

In this proposal, we will carry out experiments to test our hypothesis using human brain samples and cultured rodent neurons. Information gained from these experiments will elucidate the molecular mechanism how A $\beta$  mediates synapse loss and eventually help us design new drugs to minimize synapse loss in AD patients.

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#### **5. Immune pathology during Dengue Virus Infection**

Ashley Lauren St. John, [Emerging Infectious Diseases](#)

Dengue virus is a major world health concern, yearly impacting approximately 50 million people. In the most serious cases, infection results in severe and possibly lethal complications, such as hemorrhaging, or bleeding into the tissues. In this project we have proposed to examine Dengue virus induced vascular leakage from an immunological perspective. We will assess the contributions of various immune cells as well as several key components of immune responses to Dengue virus-induced immune pathology.

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#### **6. Dissecting the Role of the Polypromidine Tract Binding Protein in Dengue Virus Replication: A Possible Target for Small Molecule Intervention**

Azlinda Binte Anwar, [Emerging Infectious Diseases](#)

Dengue virus (DENV) is currently the most prevalent mosquito-borne viral disease in humans. Despite approximately 3.6 billion people at risk, there are currently no commercial vaccines or anti-viral drugs available to treat dengue diseases. Difficulties in developing these interventions are, in part, due to a lack of understanding of the dengue virus replication cycle in human cells. Hence understanding how host cell proteins interact with the viral nucleic acids, and their role in virus replication, is important.

The polypyrimidine tract-binding protein (PTB) is a nucleic-acid binding protein that is required by

the poliovirus, encephalomyocarditis virus and HCV for replication. We have earlier demonstrated that PTB is required for dengue virus production. In this project we aim to systematically examine the involvement of PTB in dengue virus RNA replication in human cells. The information obtained at the end of the project will form the basis for the development of rational small molecule-based therapeutics against DENV infections

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