



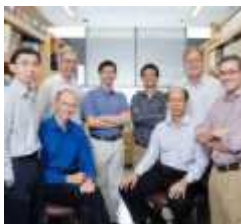
## Highlights



### Duke-NUS congratulates the graduating Class of 2012

It was with a mixture of joy, relief and bittersweet nostalgia that students from Duke-NUS Graduate Medical School donned their graduation gowns and were formally welcomed into the medical fraternity by their peers and mentors on May 26...

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### Duke-NUS genomics platform: unlocking the genome

A state-of-the-art genomics platform at Duke-NUS is opening up new horizons for research, allowing researchers to ask more refined questions and explore theories that can potentially impact the way diseases are identified, treated and cured.

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### Taking academic medicine further

Two new collaborative platforms at Duke-NUS aim to further the impact of academic and research collaborations - the Academic Medicine Education Institute to raise the level of teaching and learning and the Academic Medicine Research Institute to enhance research.

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## News In Brief

- Doctors paying it forward
- Inaugural World Autism Awareness Day launched in Singapore
- Visitors from around the world

## Research News

- Difficulty with distraction when sleep deprived
- Worksite health promotion study launched
- Partnership pays off with HFMD vaccine development
- Duke-NUS' student publishes major paper
- Prof. Mariano Garcia-Blanco receives Duke University award

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## On the long road to service

As a young boy Vincent Oei struggled with English – at the expense of his other subjects. Concerned, his mother signed him up for the Chinese Development Assistance Council's (CDAC) tuition program...

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**FYI:**

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Graduating Class of  
2012

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World Autism  
Awareness Day  
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## VITAL SCIENCE

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

*Our banner story: Our Class of 2012 graduands, Jing Wei, Ken, Jiajun, Ming Hui, Esther, Pei Ling and Fransisca, celebrate a new chapter of life as doctors. Read about their journey in "[Duke-NUS congratulates the graduating Class of 2012](#)".*

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## Duke-NUS congratulates the graduating Class of 2012

It was with a mixture of joy, relief and bittersweet nostalgia that students from Duke-NUS Graduate Medical School donned their graduation gowns and were formally welcomed into the medical fraternity by their peers and mentors on May 26, 2012 at the Yong Siew Toh Conservatory of Music at the National University of Singapore (NUS).

For the second graduating class of Duke-NUS, the hooding ceremony marked the end of their four-year Doctor of Medicine (MD) training and the start of a new journey as postgraduate year one doctors. They will provide clinical care as vital members of the healthcare team who tackle increasingly challenging issues such as age-related diseases, chronic diseases and cancer. They may go on to residency programs in specialties such as Internal Medicine, Emergency Medicine, Family Medicine, Obstetrics and Gynecology, Ophthalmology, Orthopedic Surgery, Otorhinolaryngology, Pediatrics and Psychiatry, and others.

Congratulating the class of 2012 ahead of their graduation on July 7th, Professor Tan Chorh Chuan, NUS President, recognized their hard work over the course of their studies and the rigor of the Duke-NUS program. He said, "These students have been immersed in the Duke-NUS culture of excellence, boldness and imagination; and they have benefitted greatly from the innovative clinical and research training. The rigorous training and exposure will enable our graduands to make a real difference to patients, our community and society. We are confident these graduands will become role models for future generations of clinicians and clinician-scientists who will transform medicine through research and innovation."

Mr Heng Swee Keat, Minister for Education, observed that, "Duke-NUS produces doctors with a diversity of insights and perspectives, and brings together different strengths and expertise to continually innovate and improve on the healthcare provision for Singaporeans."

Dr. Victor Dzau, Chancellor for Health Affairs, Duke University, and CEO, Duke University Health System, who visited Singapore to grace the hooding ceremony, called on the graduands to make the most of their unique skillset to serve others and to become healthcare and research leaders of the future. "Never before has there been as great a need for clinician-scientists who can not only engage in discovery science, but can translate discoveries from the laboratory to the clinic and improve the health of patients and the community," he said, "I have great pride and expectations for the class of 2012."

Urging graduands to take up the mantle of medical excellence, Professor Ranga Krishnan, Dean of Duke-NUS said that "I am proud to see that our graduands are starting a new chapter in their lives. They will work as critical members of clinical healthcare teams, to bring hope and relief to patients and their families. We hope they will continue to let their passion for medicine and their spirit of inquiry and curiosity drive future discoveries in patient and disease management," he said.

Since August 2007, Duke-NUS has had five annual intakes for its MD program and admitted more than 240 post-baccalaureate students into its American-styled, research-oriented, four-year medical school program. All Duke-NUS graduates will receive a joint Duke and NUS MD degree.

In addition to a 240-strong MD cohort, the school has over 20 students in its PhD program track that enables research-oriented students to use their biomedicine knowledge to spur translational research that develops better patient treatment, strategies and technology.

**View gallery:**



Class of 2012 Hooding Ceremony



The M.D. Class of 2012 and senior faculty from NUS, Duke and Duke-NUS. Front row: Minister Heng Swee Keat (in red robe), Dean Ranga Krishnan and keynote speaker, Prof. Sydney Brenner (in peach-colored robe).





He's all smiles. Dr. Ignasius Jappar who won five prizes, received his certificate from Dean Ranga Krishnan (left) and Minister Heng Swee Keat (right).



Dean Ranga Krishnan presents Minister Heng Swee Keat with a memento.



Duke-NUS Class of 2011 alumnus and SMA Council Member, Dr. Chia Ghim Song, attended the event with Mrs Chia. On right: Ms Corinna Cox (Duke-NUS).



Duke senior leaders Prof. Victor Dzau (left) and Prof. Michael Merson (in yellow tie) flew in to town for the event. Seen here with Mrs Melanie Chew, Nobel Laureate Prof. Sydney Brenner, Mrs Ruth Dzau, Duke-NUS Chairman Mr Tony Chew and NUS Provost Tan Eng Chye.



Vice Dean (Education) Prof. Bob Kamei with the new postgraduate year one doctors.





NUS President Tan Chorh Chuan with graduands, Dr. Bryan Ho Shihan and Dr. Ong Shin Yeu and their families.



It's a proud day for Senior Associate Dean (Education) Dr. Sandy Cook, as another class prepares to graduate.



Thumbs up for Duke-NUS!

### Interesting facts about the M.D. Class of 2012

- Average age: 24 years
- 9 students hold Masters or PhD degrees
- More than half the class has undergraduate degrees in Biology, Life Sciences, Sciences and Natural Sciences
- 11 had earlier training as engineers
- 5 studied the Social Sciences and Humanities such as anthropology, history, statistics, epidemiology and the arts
- 4 have degrees in Psychology and another 2 hold Business degrees
- Undergraduate and postgraduate institutions: National University of Singapore, Nanyang

Technological University; Fudan University, Peking University, Shanghai Jiao Tong University, Chinese University in Hong Kong; University of Mumbai; University of Philippines; University of Cambridge, University of Oxford; Duke University, Harvard University, Johns Hopkins University, Yale University

### Some achievements of the Class of 2012

- Received SingHealth Graduation Awards - [Recognizing the best of 2012](#)
- The class scored significantly higher than the U.S. national average on the Basic Science Exam (Step 1) and higher than the U.S. national average on the Clinical Knowledge Exam (Step 2CK) for the United States Medical Licensing Examination (USMLE)
- Drs. Esther Chang, Ken Goh, Foo Li Lian, Yong Ming Hui, and Cheryl Lin won research, poster and oral presentation awards in Singapore and in the U.S.
- Dr. Christina Jelly was in the Duke team that presented their recommendations to improve the social health of refugees in the Emory Global Health Case competition
- Led and organised numerous community service projects including health screening for the needy, young and elderly in Singapore, Indonesia and Thailand, and Camp Simba

## Reflections

### Celebrating the Class of 2012



"We are confident the intensive and rigorous training at Duke-NUS has not only equipped you to think critically and creatively when faced with the challenges and complexities of medical practice today, but also enabled you to galvanize your diverse talents for an impactful, collaborative approach to patient care. These attributes will distinguish you as you grow to become leading clinicians and clinician-scientists in the community."

*Prof. Ranga Krishnan  
Dean, Duke-NUS Graduate Medical School Singapore*





*Prof. Bob Kamei (right) with Dr. Tay Wei Lin  
(2<sup>nd</sup> from right) and her family members*

"Dear Class of 2012

One of the most memorable times in my entire career as an educator was when I was surprised by your class during my session in the Body and Disease Course. You can't imagine my delight when I saw signs thanking me for my work setting up the school instead of revealing your answers! I should have given you all double bonus points for that!

It has been a real pleasure and honor to know you during these past years - I will treasure watching your medical careers blossom in the future and proudly admire your contributions to care for and improve the lives of others."

*Fondly,  
Robert K. Kamei, Vice Dean, Education*



*Nicodemus (right) with Dr. Kizher Buhary (center)  
and Benjamin Farah (left)*

"The great friendships and bonds we made will withstand the test of time and as we go on our paths to become clinicians and clinician-scientists, we will look back to our days of medical education as some of the best days of our lives. Classmates you were, but more than that you shall be, from now going forward to a bright tomorrow. Congratulations and of course, looking forward to working under you in the near future."

*- Nicodemus Oey, MD-PhD Candidate, reflecting on his journey with the Class of 2012*



*Duke-NUS faculty, Dr. Sandy Cook and Prof. Pierce Chow,  
with Dr. Kaavya Narasimhalu, a SingHealth Internal Medicine resident (center)*

"It was not always easy for us and we didn't always get everything right-but we got you right. Live up to your hopes and dreams as well as ours - and be the ones who help make things better. Congratulations!"

*- Dr. Sandy Cook, Senior Associate Dean, Education*



*Mrs Dee Stenberg, Dr. Craig Stenberg, Dr. Divya Ajay,  
a Duke Surgery resident (corner right), and her mother*

"I vividly remember the day you arrived at Duke-NUS. You were so bright-eyed and earnest, and eager to pursue your dreams. As Deans, it is our goal to foster a student culture where people are valued, and you are."

*- Dr. Craig Stenberg, Assoc. Dean, Student Affairs*

## Celebrating Achievements

### Honors at the International Stroke Conference 2012



*Dr. Cheryl Lin (Duke alumna) and her parents with Duke's Prof. Victor Dzau (second from right) at the Awards Gala Dinner*

Earlier this year, Dr. Cheryl Lin, a former Duke alumna and Tufts Medical Center resident, received the American Heart Association/American Stroke Association's "Stroke Care in Emergency Medicine Award" for her oral presentation at the International Stroke Conference 2012 in February. This project was conducted during her research year. Cheryl said, "I became motivated by an interest in cardiology and guided by my mentor, Dr. Eric Peterson at Duke Clinical Research Institute (DCRI), I worked alongside Duke cardiologists and neurologists on this project."

### Major study published in journal



*(L-R): Dean Ranga Krishnan, Dr Ong Shin Yeu and Minister Heng Swee Keat*

Dr. Ong Shin Yeu, a Duke alumna, who did her third-year elective at the Singapore Eye Research Institute (SERI), has had a major paper published in Archives of Ophthalmology. This study shows that in the Singapore Malay Eye Study, older persons with poor vision, particularly from cataract, were more than twice as likely to have cognitive dysfunction. Of the specific eye diseases, diabetic retinopathy - a disorder of the retinal blood vessels that can lead to blindness in patients with long term diabetes - was independently associated with cognitive dysfunction. She was primarily supervised by Dr. Carol Cheung of the Singapore National Eye Centre and Dr. Benjamin Haaland of Duke-NUS.



## Reflections on Our Journey to Graduation



*Jiajun with his newborn baby, Edwin, and Ting  
Photo credit: Feng Jiajun*

"28th April 2012, to most of my classmates, was the day of the final exams. But for me, it was certainly much more.

My wife, Ting was admitted to the labor ward just before the exam started. I was pacing around, worried. After my exam ended, I rushed straight to the labor ward. The first thing Ting asked me which I will never forget was: "How was your exam?" I was so touched by the warmth of her words. It brought back memories of how my wife had unreservedly supported my medical education for the past four years. Just three hours after my final exam, my second son Edwin arrived.

That day marked the start of a new chapter of my life as a medical resident. It also celebrated the beginning of Edwin's life in my family. I will also remember this date for the huge significance it has for my family."

*- Dr. Feng Jiajun, SingHealth Transitional Year, NUS alumnus*



*Dr. Esther Chang received her award from Prof. Victor Dzau*

In June 2009, when I was in my first year, Camp Simba was launched by a course mate as a collaborative effort between students of Duke-NUS and the Yong Loo Lin School of Medicine. This was a June holiday camp in Sentosa for the children of cancer patients.

Through our involvement, we became more aware of the impact chronic, life-threatening illnesses

like cancer had on our patients and their families. Later on, some of the patients also shared with me both their hopes and worries for their children. The experience was very humbling and laid the foundation for our subsequent annual camps."

- *Dr. Esther Chang, Recipient of Duke-NUS Humanism Award and NUSS Medal for Outstanding Achievement, SingHealth resident in Internal Medicine and NUS alumnus*



*Eugene Stead College members on one of their outings with Dr. Michelle Jong and Dr. Janil Puthucheary and their sons; and Dr. Toh Han Chong (last row in light blue shirt). Juliet in front row, corner right. (Photo credit: Juliet Tan)*

"One of my favorite experiences of medical school is being part of the Eugene Stead College. What began as a simple tradition of weekly lunch meetings with classmates and dedicated college masters would grow into a close-knit group of friends enjoying more study parties, community projects, and group dinners than we could ever imagine.

Much of the colleges' success had to do with the vision and enthusiasm of our college masters. They were always encouraging us to take a step back and not lose sight of the big picture.

Many of us were fatigued and stressed after our clinical ward rounds, and battled a nagging sense of guilt at occasionally not being able to complete our readings or assignments.

Dr. Toh Han Chong, Dr. Michelle Jong and Dr. Michael Chee were always there to remind us to enjoy the journey of medical school, keep well and to look ahead. I will always be thankful for their advice."

- *Dr. Juliet Tan, SingHealth resident (Pediatrics) and Amherst College alumnus*



*Dr. Kizher Buhary, SingHealth resident (Orthopedic Surgery) and recipient of Duke-NUS Achievement Prize for Top Score in Second-Year Clinical Skills Examination and NUS alumnus*

"What was meant to be learnt over two years was taught over 10 months. This would have been impossible if not for excellent program coordinators like Prof. Pierce Chow, Dr. Doyle Graham and Dr. Janil Puthuchery.

My memories included my Obstetrics and Gynecology posting where I delivered a baby and the challenging Surgery clerkship where sometimes, our days were so long that we didn't see the sun rise and set.

In my third year, I worked with Prof. James Hui, an NUH pediatric orthopedic surgeon. Apart from our research discussions, we used to argue over the Barclays EPL games (Prof. Hui was an avid Arsenal fan). I also had the privilege of presenting at the European Pediatric Orthopedic Society conference in Switzerland that year.

Looking back, I would like to thank the patients I attended to over the past four years and our faculty educators who not only taught us but respected us and made us feel valued. I also thank my family and my wife for their encouragement.

Lastly, a big thank you to the Class of 2012 for being one of the best groups of friends. You all have been supportive and inspiring and I wish you the best and look forward to working with you.

The countdown is finally over. I am officially Dr. Kizher Shajahan Mohamed Buhary!"

*- Dr. Kizher Buhary*



## Congratulations from 3<sup>rd</sup>-Year Research Faculty Mentors



*Dr. Ooi, Kashfi and Prof. Duane Gubler*

"It was a privilege to work with Kashfi who designed her research project, not only out of a scientific curiosity but also out of compassion and empathy for the migrant workers in Singapore. I will follow her career keenly and look forward to the possibility of collaborating with her in the near future. Our best wishes."

*- Dr. Ooi Eng Eong, Associate Professor, Program in Emerging Infectious Diseases (seen here in photo with Prof. Duane Gubler and Kashfi (center). Dr Kashfi Qadri is an alumnus of Smith College (UK) and a SingHealth resident in Pediatrics*



"Pippa was a true professional who worked hard to make a difference in medical research. She clearly demonstrated the work ethic and intellectual acumen for a successful medical career. I wish her nothing but the best."

*- Dr. Scott A. Summers, Associate Professor, Program in Cardiovascular and Metabolic Diseases, talking about Dr. Guadalupe Cara Jimenez Vigelmann [Pippa] (left photo), alumnus of University of Philippines and a Pediatrics resident with SingHealth. Pippa received the SingHealth Prize in Family Medicine and the Singapore Medical Association-Lee Foundation Teammanship Award*

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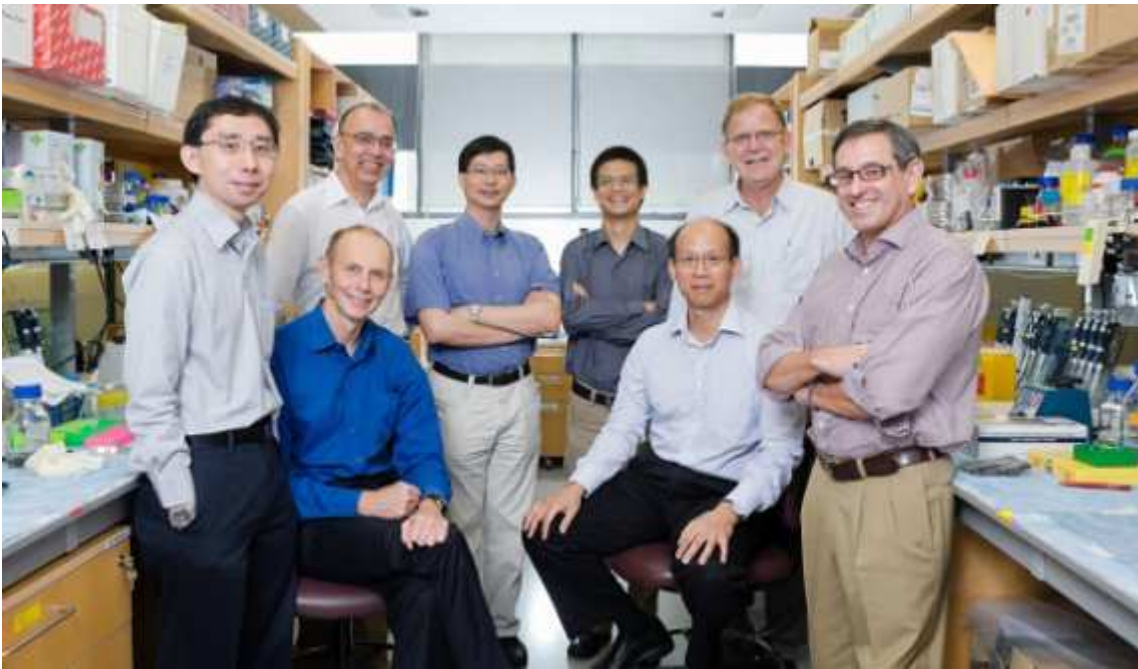
## Duke-NUS genomics platform: unlocking the genome

*A state-of-the-art genomics platform at Duke-NUS is opening up new horizons for research, allowing researchers to ask more refined questions and explore theories that can potentially impact the way diseases are identified, treated and cured.*

Genomics testing has come a long way. From the billions of dollars and decade of research that it once took to map just one human genome twenty years ago, it now takes about S\$6,500 and just four days to do the same. This has fundamentally changed the way research is being done. These new technologies have been brought into Duke-NUS, resulting in an in-house genomics platform that has given researchers the ability to initiate genomics research programs that have the potential for major impact on a multitude of disease processes.

Associate Professor Patrick Tan, Director of the Duke-NUS Genome Biology Facility (DGBF) explained, "The DGBF was established in 2008 with the mission of facilitating biomedical research through genomic technology. The school saw a need to empower small academic laboratories, particularly on the Outram Campus, with genomic technologies to drive and accelerate innovative research. Currently, DGBF has processed customer orders from all over the island, including Duke-NUS, SingHealth, NUS, and Biopolis, facilitating several projects and publications."

Professor David Virshup, Program Director for Cancer & Stem Cell Biology, noted, "The technology allows us to answer questions much more rapidly. This gives our investigators access to new cutting-edge technologies to study the genetic basis of disease. Our researchers at Duke-NUS and SingHealth are using this technology to probe questions such as what genes and mutations lead to cancer, what genes make cancers worse, what genes make one resistant to treatment, and so on."



*All in favor of the genomics platform. From left: Dr. Charles Chuah, Dr. Shirish Shenolikar, Dr. Steve Rozen (seated, in blue), Dr. Patrick Tan, Dr. Zang Zhi Jiang, Dr. Patrick Casey, Dr. Ong Sin Tiong (seated) and Dr. David Virshup*

Senior Associate Dean for Research, Professor Shirish Shenolikar, added that the DGBF has bridged a gap in the research scene and, with the school's newly-established metabolomics platform, has markedly expanded the scope for research. "The Duke-NUS facility was designed to fill a very critical gap in the progression of science from cellular and animal studies to human studies. Without this facility, we would not have the tools to do the types of focused comparative studies that are critical for our researchers to develop validated models of human disease. The goal of this platform is to allow anyone within Duke-NUS and our partners in Academic Medicine to have ready access to this important tool."

This, said Professor Patrick Casey, Senior Vice Dean for Research, gives investigators a starting point to do genomic analyses at almost any scale. "Access to this platform allows our investigators to ask deeper questions by providing much more detailed and comprehensive data on the genetic makeup of specimen, be it a cell, tissue, or tumor. Having the technology means we can pinpoint processes that go awry in disease. It is a tool to allow us to look at disease processes with a higher degree of resolution. All five of our Signature Research Programs can potentially benefit from the technology."

The four senior researchers, who have benefited from the Duke-NUS genomic platform, further noted the platform also has the benefit of making more prudent use of research investment dollars through substantial cost-savings by sharing resources established within the school. It also strengthens research collaborations between scientists, which has contributed to milestone making discoveries led by scientists at Duke-NUS, working alongside teams in and outside Singapore.

Prof. Virshup illustrated this, noting, "The platform has already made an impact. In three years, our researchers have performed studies that otherwise could not have been done. We've had three major papers published in the first half of this year alone (see box story). Access to this genomics platform means we now have a brand new way of looking at the world. We could not have done these five years ago, and today we are doing new experiments we could never have dreamed about then. These machines have transformed the way genetic experiments are done."



## Ground-breaking research from the Duke-NUS Genomic Platform

*The in-house genomic platform at Duke-NUS has resulted in several discoveries led by scientists at Duke-NUS and has strengthened research collaborations with teams in and beyond Singapore.*

### East Asian gene variant discovered to cause resistance to cancer targeted therapy

Duke-NUS and SGH cancer researchers, Drs. Ong Sin Tiong and Charles Chuah, together with a multinational team, have identified a variation of the BIM gene that explains why some patients fail to benefit from highly-effective cancer drugs called tyrosine kinase inhibitors (TKIs).

In the study, which was led by Dr. Ong, an Associate Professor in the Cancer and Stem Cell Biology Signature Research Program at Duke-NUS and Division of Medical Oncology at Duke University Medical Center in the US, genome sequencing technology was used to look for structural changes in the DNA of patient samples. Using this approach, they discovered the BIM gene variant among patients who were resistant to TKIs but not in those who were sensitive. Interestingly, the BIM gene variant was commonly found (~15% incidence) in individuals of East Asian descent (Chinese, Japanese, and Koreans), but was completely absent in Caucasians and Africans. The study, published online in *Nature Medicine* on March 18, is significant, said Dr. Ong, "Because knowing about the effects of the gene variant allows for better identification of patients who are more likely to respond poorly to TKI therapy. In this way, we will be able to personalize therapy for these patients to avoid ineffective therapies that could be toxic and expensive, and test out new strategies to prevent TKI resistance from developing."

Having identified the mechanism by which the BIM variant caused drug resistance, the team predicted that another class of cancer drugs, called 'BH3 mimetics', would be able to overcome it. Dr. Ong said: "When the BH3 mimetic drugs were added to TKIs in cancer cells with the BIM gene variant, we were able to overcome the resistance conferred by the gene. Our next step will be to bring this to clinical trials with patients."



*Without his DNA helix bowtie, the gingerbread in the middle realizes he has the BIM deletion polymorphism, and hence less likely to respond well to medication.*



*The genomics platform in action*

### **Critical stomach cancer genes identified**

The identification of hundreds of mutant genes in stomach cancer may help doctors improve the customization of cancer treatments. The study, led by Duke-NUS in collaboration with the National Cancer Center Singapore (NCCS) and international partners, discovered the gene mutations by analyzing both normal and tumour tissues from stomach cancer patients using DNA sequencing technology. Out of the 18,000 genes studied, they found more than 600 genes that were previously unknown to be mutated in stomach cancer. Two genes called FAT4 and ARID1A were found to be particularly significant. These genes were mutated in 5 and 8 per cent of stomach cancers, respectively. According to Assoc. Prof. Patrick Tan, the senior author of the study from the Cancer and Stem Cell Biology Program at Duke-NUS and who is affiliated with the Cancer Science Institute of Singapore, and

A\*STAR's Genome Institute of Singapore, this newfound knowledge may help lead to more effective treatment of stomach tumors and other cancers. In addition, senior co-author Assoc. Prof. Steven G. Rozen, Ph.D., who heads the Computational Systems Biology and Human Genetics Laboratory in Duke-NUS, noted, "This technology allows us to read the DNA sequence of the protein-coding genes in each cancer genome for less than US\$2,000 (SGD\$2,500), an incredibly low price." The findings were published online on April 8 in *Nature Genetics*.

### **New gene mutations implicated in bile duct cancer**

Researchers from Duke-NUS, the National Cancer Center of Singapore (NCCS) and Khon Kaen University in Thailand have used state-of-the-art genomic technologies to discover that new gene mutation that occur in bile duct cancers, or cholangiocarcinoma. Researchers analysed eight bile duct cancers and normal tissues from Thai patients, and discovered mutations in 187 genes, including genes such as MLL3, ROBO2 and GNAS, that have not been previously implicated in bile duct cancers. The researchers also compared bile duct cancers to other related cancers of the liver and pancreas and found that the bile ducts cancers shared similarities with pancreatic cancer.



*Prof. Teh Bin Tean, lead researcher for the breakthrough in bile duct cancer gene mutation*

This finding, said lead researcher Professor Teh Bin Tean, Director and Principal Investigator of the NCCS-VARI Translational Cancer Research Laboratory at the NCCS and professor at Duke-NUS, paves the way for better understanding on how bile duct cancers develop. "This discovery adds depth to what we currently know about bile duct cancer. More important is that we are now aware of new genes and their effects on bile duct cancer and we now need to further examine their biological aspects to determine how they bring about the onset of cholangiocarcinoma." The discovery was published on May 6 in *Nature Genetics*.

Bile duct cancer is a fatal form of cancer that accounts for 10 to 25 per cent of all primary liver cancers worldwide and is prevalent in Southeast Asia, particularly Northeast Thailand. The

cancer is caused by long-term consumption of raw fish infected with liver flukes (a type of parasite found in fish). When eaten, the flukes accumulate in the bile ducts of the human host, causing constant infection and the onset of cancer.

For more information regarding DGBF services and collaborations, please contact Assoc. Prof. Patrick Tan at [gmstanp@duke-nus.edu.sg](mailto:gmstanp@duke-nus.edu.sg) or Ms Angie Tan at [angie.tan@duke-nus.edu.sg](mailto:angie.tan@duke-nus.edu.sg). Some DGBF equipment was purchased by a grant from the Cancer Science Institute of Singapore.

## What is genomics?

Genomics is the study of deoxyribonucleic acid (DNA) - the hereditary material in our cells that forms the blueprint for the body and its functions. While other factors such as diet, lifestyle, and environmental factors also play a role in disease prevention and management, the study of genetics helps improve the understanding of one part of the big picture. Genomics is aimed at understanding the role our genes play in how and why diseases occur. Understanding genomics helps researchers to develop more effective diagnostic and treatment tools that are based on an individual's unique make-up.

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## Taking academic medicine further

*Two new collaborative platforms at Duke-NUS aim to further the impact of academic and research collaborations - the Academic Medicine Education Institute to raise the level of teaching and learning and the Academic Medicine Research Institute to enhance research.*

Bringing together clinical care, education and the development of new knowledge, Academic Medicine at Duke-NUS and SingHealth has taken on an added dimension with the launch of two new platforms: the Academic Medicine Education Institute (EI) and the Academic Medicine Research Institute (RI).

According to Professor Bob Kamei, Vice Dean of Education at Duke-NUS, "The EI is a way to bring together the mutual strengths and expertise within Duke-NUS and SingHealth. This allows us to reach a wider audience of faculty staff and other learners with the concept called Academic Medical Education."

He explained, "Academic Medical Education is not only about improving the way we teach healthcare learners across the spectrum, from doctors, nurses, allied healthcare professionals, but also the way they learn. It's an additional slant on education that seeks to improve teaching or learning skills. In addition, Academic Medical Research is about doing the studies that change the way we care for people and the bigger the impact on people's health. The quality of every discovery is measured by the impact it has on people's lives. In the same way, greater the impact you make in education, the greater the advancement in medical research."

Ultimately, it is about improving the way teaching and learning in a way that brings about the greatest impact. This means not just training individual students, but also through broader means such as course writing, resident programs and educational medical research, all of which develop people to reach their full potential for the benefit of medical science and patients, added Prof. Kamei.

Similarly with the AMRI, Professor John Rush, Vice Dean, Clinical Sciences, the idea is to



*Clinician-scientists discussing their research*



*Prof Bob Kamei, Vice-Dean (Education)*



*Prof John Rush, Office of Clinical Science*

develop strong research careers and expertise, support people engaged in research and the pursuit of independent research funding.

"We provide enabling structures and functions in order to help execute research. In having an academic home, people can talk about ideas with each other, think through things and try innovations through being exposed to new ideas."

He added, "The days of doing research alone in a lab are gone. We are looking at improving scientific collaborations across a wider scale

and scope. To understand a disease these days, we need a multidisciplinary team, from biochemists, radiologists, geneticists, statisticians, metabolomics, proteomics and disease experts." Other resources also range from workshops to help develop protocols and grant applications, access to quantitative expertise (in biostatistics, epidemiology or bioinformatics) and mentorship to peers with whom researchers can collaborate with to help shape protocols and develop safe, efficient and clear research.

"The RI also provides functions such as medical writing reviews, assistance in data capture, consultation with experts from Duke (Durham, USA) and elsewhere," said Professor Rush. "We want to make the research process easier, more feasible, less painful and more fun. The aim is to develop careers through creativity and collaboration to contribute the best outcome to patients."

## Academic Medical Research

**Translational research:** The study of how bodily functions and diseases work in people through the study of animal models. Translating studies done or information gathered on animals to human application. In translational medicine, researchers may find drug targets or physiological systems that can be modified with medicines or behavior change.

**Clinical research:** Taking the data found in translational research and applying them to patients to see if these treatments work, for whom it works and when in the course of a disease it is most effective to discover how a treatment or diagnostic test is best applied in practice.

**Health services:** The study of clinical applications and analysing what is the most cost effective and effective way to deliver a new treatment.

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#### HIGHLIGHTS

- ▶ Duke-NUS congratulates the graduating Class of 2012
- ▶ Duke-NUS genomics platform: unlocking the genome
- ▶ Taking academic medicine further
- ▶ On the long road to service

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## On the long road to service

As a young boy Vincent Oei struggled with English - at the expense of his other subjects. Concerned, his mother signed him up for the Chinese Development Assistance Council's (CDAC) tuition program. That was where Vincent met Dr. Syed Yusof, an inspiring figure who became Vincent's tutor and mentor. Using innovative teaching methods, Dr. Yusof piqued the young student's interest in the English language and improved Vincent's vocabulary by taking the time to teach and explain root words to expand his comprehension. Under Dr. Yusof's tutelage and guidance, Vincent eventually scored an A2 for his GCE 'O' Level examinations which led him to receive the CDAC Achievement Award in 2002. "Now, as a medical student, I still use his methods to figure out the meanings of unfamiliar words," Vincent shared.

His struggle with grades didn't daunt Vincent's aspiration to be a clinician-scientist, a dream fuelled in part by the illness and early demise of his father. But that journey too was not without obstacles. A C6 for his General Paper for his GCE 'A' Level examinations made Vincent ineligible to qualify for local medical school. Vincent took up Biomedical Science instead, during which he went on an exchange program at to Sweden's Karolinska Institute where he was "greatly inspired" by its programs for innovation and clinician-scientists. "I decided to pursue a career in Medicine." It was also in Sweden that he met another mentor and role model, Dr. Petter Brodin, MD-PhD, who spurred him to add Medicine to his initial plan of pursuing a PhD.

Helping him in this arduous journey was an A\*STAR's Pre-Graduate Scholarship – a financial grant that relieved the financial burden of supporting his studies and living expenses. Upon completion of his degree, Vincent successfully applied for a place in Duke-NUS Graduate Medical School. It was a choice inspired by a speech made by Professor Bob Kamei during an introduction session. "Duke-NUS' student-oriented and innovative pedagogy of engaging and developing students to apply their knowledge in medicine appealed to me," Vincent said.



*Second-year student Vincent Oei*

Today, Vincent is in his second year as a candidate in the MD/PhD program and has benefitted from a Duke-NUS Bursary. Being a beneficiary of financial aid and as a way of giving back, Vincent is also an avid and enthusiastic volunteer of Tan Tock Seng Hospital's Community Health Engagement Program (CHEP). He goes down to Thye Hua Kwan Moral Society Seniors' Activity Center in Toa Payoh twice a month to conduct an exercise program. There, he helps the elderly with their mobility and improve their ambulation.

Dr. Craig Stenberg, Associate Dean, Student Affairs & Admissions, has this to say of Vincent, "Vincent is a person who really gives back. He has been very active in community service and



has worked tirelessly with our recruiting team helping to attract outstanding students to Duke-NUS."

To recognize Vincent's achievement of coming out tops in his CDAC year, he is featured in the CDAC's 20th Anniversary [YouTube video](#) and commemorative book.

With eight more years of study and a housemanship to complete before he becomes a doctor, Vincent knows his long journey is far from over. But he draws strength from his experiences, not in the least from his time with the CDAC tuition program. "It gives me faith that with hard work and tenacity, anything is possible."

To date, about 70% of all Duke-NUS students receive some form of financial aid. This is Duke-NUS' commitment that no talented student like Vincent is denied of the opportunity to fulfill their medical aspirations as clinician-scientists, and to contribute back to the community by transforming medicine and improving lives.

Make a gift now to our **Student Financial Aid Fund**, via our website: [www.duke-nus.edu.sg/giving](http://www.duke-nus.edu.sg/giving), or call 6516 2585 to discuss your gift.

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NEWS IN BRIEF

- ▶ Doctors paying it forward
- ▶ Inaugural World Autism Awareness Day launched in Singapore
- ▶ Visitors from around the world

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Prof. Pierce Chow

## Doctors paying it forward

What can grateful doctors do to pay it forward? Some give their time and money to causes, while others give back by sharing knowledge and experience to multiply the impact of medicine and science. At Duke-NUS, understanding and conducting research is an important component of the medical training program. As such, medical students are encouraged to attend medical symposiums and showcase their research findings at conferences for peer reviews. These provide invaluable exposure which surpasses classroom training. Initiated by a doctor in 2009, the Doctors-for-Doctors Fund allows doctors to support young clinician-scientists in training by helping with the expenses incurred from overseas attachments and conferences.

We asked Prof. Pierce Chow about his thoughts on paying it forward:

### 1. Why do you think the ethos of 'paying-it-forward' is important?

In the context of a medical profession where the training takes years, the only way we can repay our own teachers is to pay it forward – the way our teachers did for us for many years.

### 2. How else can doctors give to future doctors besides monetary donations to student financial aid?

Besides the ability to give monetary aid to fellow future doctors, the other important thing that doctors can give to future doctors is time – time to serve as teachers, research supervisors and mentors to junior doctors. No one else can carry out these roles well except doctors themselves.

### 3. Besides, treating patients, why is it important for doctors to be involved in philanthropy or community services?

Clinical work fulfills an important part of the healing spectrum, but by itself, it is incomplete. The patient is part of a family and community and healing can only be completed within that context and environment. We have the ability to be more engaged in helping society. Being involved in philanthropy and community service completes the healing spectrum.

Make a contribution to our **Doctors-for-Doctors Fund** which provides financial assistance to medical students attending overseas conferences and attachments.

Log on to [www.duke-nus.edu.sg/giving](http://www.duke-nus.edu.sg/giving) or contact the Development Team at 6516 2585 to make a gift.

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*Volunteers Cheery in Blue!*

## Inaugural World Autism Awareness Day launched in Singapore

The United Nations General Assembly declared the second day of April, World Autism Awareness Day (WAAD). This year, students from Benjamin Sheares College, Duke-NUS, had the privilege of collaborating with five autism centers in Singapore to organize activities for WAAD 2012. These were: Autism Association (Singapore), Autism Resource Center (Singapore), Rainbow

Center, Shoulders Singapore, and St. Andrew's Autism Center. Our campaign included two concurrent one-day seminars for caregivers and healthcare professionals, as well as participation in the global *Light It Up Blue!* for Autism Campaign.

This year marked Singapore's inaugural participation in the *Light It Up Blue!* campaign together with the mall owner of ION Orchard. The massive shopping mall located in Orchard Road was lit in a cheery shade of blue on 30 March, and garnered much attention from tourists and pedestrians alike. Volunteers had gathered at ION Orchard earlier in the day to distribute collaterals to raise awareness and spread the word about autism.

Our school had also participated in the *Light It Up Blue!* campaign on a smaller scale.

The following day, two parallel seminars were organized. For caregivers, the theme of the seminar was 'Transition into Adulthood', an important topic for parents to gain more knowledge as they make future plans for their child with autism.

For the healthcare professionals, Dr. Alvin Liew from the Institute of Mental Health (IMH) talked about the implications of the Diagnostic and Statistical Manual of Mental Disorders' fifth edition (DSM-V), while Dr. Mariam Aljunied from the Ministry of Education provided insights into how to approach children with autism.

WAAD 2012 was a truly meaningful endeavor. It was indeed our privilege to be a part of this worthwhile cause. We are deeply appreciative of everyone who gave up time, energy and encouragement to make the event possible. A special note of thanks also to our college masters and seniors, whose time, efforts, guidance and insights were invaluable.

Contributed by:

Debra Quek and Anu Pandey

Benjamin Sheares College

Duke-NUS Graduate Medical School



**View gallery:**



Volunteers Cheery in Blue! - (L-R): (back row) Beau Fenner, Chester Huang, He Song, Agnes Chao, Alfonso Tan-Garcia, Poh Yen Yeong; (second row) Sashen Aponso, Zhou Yi, Shayna Siew, Robyn Hay, Assoc. Prof. Paul Yen; (front row) Xiong Jiaqing, Sumitro Harjanto.



All ready and raring to go out there to spread the word about Autism - (L-R): Alfonso Tan-Garcia, Xiong Jiaqing, Zhou Yi, Poh Yen Yeong.



Sharing the message of Autism Awareness with the young.



Assoc. Prof. Paul Yen (in blue) getting youths involved with Autism Awareness.



The crowd gathers in support of WAAD.





Countdown to the Light Up - (L-R): Mr Yew Teng Leong (President of Rainbow Centre Singapore), Ms Sylvia Yap (Autism Resource Centre), Ms Denise Phua (MP of Moulmein-Kallang GRC, President of the Autism Resource Centre and co-founder of Pathlight School), Mr Sam Tan (Mayor of Central Singapore CDC and MCYS Senior Parliamentary Secretary).



Distinguished guests at the event - (L-R): Ms Sylvia Yap, Mrs June Tham (Executive Director of Rainbow Centre), MP Denise Phua (President of the Autism Resource Centre and co-founder of Pathlight School), Dr. Craig R Stenberg (Associate Dean, Student Affairs & Admissions, Duke-NUS), Mr Yew Teng Leong (President of Rainbow Centre Singapore), Mr Sam Tan (Mayor of Central Singapore CDC and MCYS Senior Parliamentary Secretary), Mr George Young (local artiste).





ION Orchard Lights Up Blue for World Autism Awareness Day 2012.



Opening Speech by Dean Ranga Krishnan.



Keynote Address by Heads of Autism Centres - (L-R): MP Denise Phua, Mr Yew Teng Leong and Mr Dennis Ang.



Joint panel discussion - (L-R): Ms Ang Bee Lian, Ms Loh Wai Mooi, Ms Denise Phua, Dr Mariam Aljunied and Dr Alvin Liew.



Many thanks to all who made the seminars possible! - (L-R): Mr Dennis Ang, MP Denise Phua, Prof. Kon Oi Lian, Mr Yew Teng Leong, Ms Loh Wai Mooi, Ms Ang Bee Lian, Dr. Mariam Aljunied, Dr. Alvin Liew and Ms Wong Yeok Lin.

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**22 February 2012: Southern Denmark's Regional Council**

*Dean Ranga Krishnan, Senior Vice Dean (Research)  
Patrick Casey and Associate Dean (Learning)*

## Visitors from around the world

In just over a month, Duke-NUS welcomed close to 80 visitors who wanted to learn more about the school's research and medical education areas. Among them are His Excellencies, Pehin Dato Haji Adanan Yusof (Brunei's Minister of Health) and Pehin Abu Bakar Apong (Brunei's Minister of Education), Mr. Carl Holst (Vice-President of the Danish Region) and their accompanying delegates.

In early March, we also hosted 60 educators and faculty members from various universities in Asia



Technologies) Frank Starmer hosted the visit by President of the Regional Council of the Region of Southern Denmark, Mr. Carl Holst (front row, 2<sup>nd</sup> from left) and his delegation.



**22 February 2012: Southern Denmark's Regional Council**

Prof. Patrick Casey, Senior Vice Dean (Research) briefs the President of the Regional Council of Southern Denmark, Mr Carl Holst and his delegates on Duke-NUS' five signature research programs.

under the Temasek Foundation-NUS Leadership Program.

"The journey to building a school is truly exciting. As much as our visitors come to learn from us, we also learn from them in the process" says Prof Ranga Krishnan, Dean of Duke-NUS.



**5 March 2012: Educators from Asian Universities**

Duke-NUS gave a warm welcome to the 60 educators and faculty members from various universities in Asia under the Temasek Foundation-NUS Leadership program.



**21 March 2012: Minister of Health, Brunei**

His Excellency, Pehin Dato Haji Adanan Yusof (4<sup>th</sup> from left) and his delegates with Vice-Dean (Education) Bob Kamei (in white shirt) at the end of the campus tour.



**5 April 2012: Minister of Education, Brunei**

We were much honored to host His Excellency, Pehin Abu Bakar Apong (2<sup>nd</sup> from left). Photo: Associate Dean (Corporate Services) Ms. Karen Chang and Vice-Dean (Education) Bob Kamei (in white shirt).

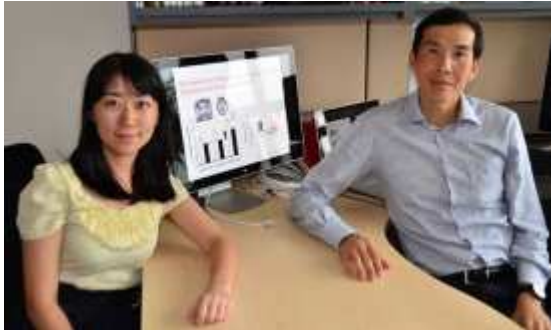
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RESEARCH NEWS

- Difficulty with distraction when sleep deprived
- Worksite health promotion study launched
- Partnership pays off with HFMD vaccine development
- Duke-NUS' student publishes major paper
- Prof. Mariano Garcia-Blanco receives Duke University award

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Kong Danyang and her supervisor, Prof. Michael Chee

## Difficulty with distraction when sleep deprived

It's been a long night but at the security check-point, officers need to stay vigilant. A wily troublemaker is about to slip in some dangerous cargo disguised among harmless items that would normally be passed over in an inspection.

So how does one hone the attention span to be able to detect a target item and ignore distractors? Graduate student Kong Danyang

researched this intriguing area of selective attention at the Cognitive Neuroscience Lab (CNL) under the supervision of Professor Michael Chee, a principal investigator with the Duke-NUS Neuroscience and Behavioral Disorders Program.

Danyang, a scholar in the NUS Graduate School of Integrative Science and Engineering program, has been researching the brain's information processing limits under conditions of acute total sleep deprivation. In prior work, she found evidence for a reduction in 'left-over' visual processing capacity when one has to focus on a central task. Using fMRI, she was able to demonstrate that loss of capacity can be evaluated without the participant's awareness.

Extending this finding in work that was published in the journal *Neuroimage* earlier this year, Danyang presented her sleep-deprived volunteers with overlapping pictures of faces and houses and had them focus either on faces, houses or to passively view the stream of images. She found that the ability to enhance the brain's representation of target objects can be relatively preserved in sleep-deprived persons. However, the brain is less able to suppress the distracting image. This finding resembles the results of research on cognitive aging where difficulty with suppressing distractors is a well-known feature.

"Danyang's work contributes to our understanding about why cognitive performance - and in particular attention - declines when we pull all-nighters," said Prof. Chee. "The research, which gives a clearer understanding of why cognition fails, provides specific targets to evaluate countermeasures. While we advise persons to get sufficient sleep at night, it is difficult to escape sleep loss when people are as busy as most city dwellers are. The research conducted at the CNL provides scientists principled ways of evaluating countermeasures and training to reduce deficits. At the very least, we can apply such tests on person who would compromise the safety and well-being of others if they encounter total sleep deprivation," he added.



## Worksite health promotion study launched

A Duke-NUS health researcher, Assoc. Prof. Eric Finkelstein, has launched a major study with the Health Promotion Board to test an innovative worksite health promotion program. Employees will use smartphones to log their workouts. If they meet their weekly exercise activity goal, they may earn cash incentives or raise money for a charity of their choice. Grounded on cutting-edge economic theories and behavior change techniques, this program has the potential to bring about long-term behavior change among employees and cost-savings for employers.

For information, please visit: [http://hssr.duke-nus.edu.sg/idat\\_plus](http://hssr.duke-nus.edu.sg/idat_plus) or call: 6601 2450.

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## Partnership pays off with HFMD vaccine development

It is only slightly more than a year but the partnership between Duke-NUS and Inviragen formed in 2011 has paid off. In just six months, the first phase of a study that could possibly create a vaccine for the Hand, Foot and Mouth Disease (HFMD) was initiated and completed with great success. HFMD is caused by the enterovirus 71 (EV71) and is a common epidemic among children especially in Southeast Asia.

The study involved 36 healthy adults who were provided with two either high or low-dose immunizations of the INV21 vaccine each. INV21 is Inviragen's purified virus particle vaccine. All participants showed a significant increase in their immune responses, which could mean that they are protected from the virus. "We were able to initiate this study rapidly and complete it in only six months through a productive relationship with the Singapore National University Health System (NUHS) and our collaboration with Duke-NUS Graduate Medical School," said Dr. Joseph Santangelo, Inviragen's chief operating officer.

While more clinical trials will be conducted later this year to determine the vaccine's safety and ability to provoke an immune response in children, the vaccine may be available in the market in 2015.

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## Duke-NUS' student publishes major paper

Ms Ong Shin Yeu, a Duke-NUS Class of 2012 medical student who did her third-year elective at the Singapore Eye Research Institute (SERI), has had a major paper published in Archives of Ophthalmology. She was primarily supervised by Dr. Carol Cheung of the Singapore National Eye Centre and Dr. Benjamin Haaland of Duke-NUS. This paper shows that in the Singapore Malay Eye Study, older persons with poor vision, particularly from cataract, were more than twice as likely to have cognitive dysfunction. Of the specific eye diseases, diabetic retinopathy—a disorder of the retinal blood vessels that can lead to blindness in patients with long term diabetes—was independently associated with cognitive dysfunction.

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*Prof. Mariano Garcia-Blanco*

## **Prof. Mariano Garcia-Blanco receives Duke University award**

Every year, Duke University awards distinguished professorships to its faculty. This year, Professor Mariano Garcia-Blanco was named the Charles D. Watts Professor of Molecular Genetics and Microbiology. He is also a Professor and Principal Investigator in the Laboratory of Molecular Virology of the Emerging Infectious Diseases program at Duke-NUS.

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GRANTS AWARDED

- ▶ Development of multiplex-FISH assays for selection of subtype-specific therapies in gastric cancer tissues and circulating tumour cells
- ▶ Domains of health-related quality of life important and relevant to cancer palliative care patients in Singapore: A preparatory study for the development of an item bank
- ▶ A critical role for mast cell responses in pathophysiology of the dengue infections
- ▶ Characterization of induced-pluripotent stem cell-derived cardiomyocytes from patients with arrhythmogenic right ventricular cardiomyopathy for potential use as a diagnostic test
- ▶ Investigation on sensitivity and specificity among protein biomarkers of acute decompensated heart failure and in comparison with "biomarker protein profile" and novel circulating biomarkers
- ▶ Human iPS cell-derived MSCs as an important alternative cell source for the cardiovascular cell therapy of older and sicker patients
- ▶ Evolutionary consequences of reassortment on influenza A virus

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Details of projects awarded to Duke-NUS researchers.

No.	PI	Dept	Project Title (Please click titles for details)	Grant Call	Duration (Months)
1.	Kakoli Das	CSCB	Development of multiplex-FISH assays for selection of subtype-specific therapies in gastric cancer tissues and circulating tumour cells	SCS Cancer Research Grant 2011	12
2.	Cheung Yin Bun	CQM	Domains of health-related quality of life important and relevant to cancer palliative care patients in Singapore: A preparatory study for the development of an item bank	Lien Centre for Palliative Care Extramural Research Award	12
3.	Soman Abraham	EID	A critical role for mast cell responses in pathophysiology of the dengue infections	Merlion Programme 2011	24
4.	Reginald Liew	CVMD	Characterization of induced-pluripotent stem cell-derived cardiomyocytes from patients with arrhythmogenic right ventricular cardiomyopathy for potential use as a diagnostic test	Goh Cardiovascular Research (GCR) Award	24
5.	David Sim	CVMD	Investigation on sensitivity and specificity among protein biomarkers of acute decompensated heart failure and in comparison with	Goh Cardiovascular Research (GCR) Award	24

			"biomarker protein profile" and novel circulating biomarkers		
6.	Wei He Ming	CVMD	Human iPS cell-derived MSCs as an important alternative cell source for the cardiovascular cell therapy of older and sicker patients	Goh Cardiovascular Research (GCR) Award	24
7.	Vijaykrishna Dhanasekaran	EID	Evolutionary consequences of reassortment on influenza A virus	MOE Tier 2 July 2011 Grant Call	36

**Total Amount of Funding Received: \$3,143,141**

## Synopsis

### 1. Development of multiplex-FISH assays for selection of subtype-specific therapies in gastric cancer tissues and circulating tumour cells

Kakoli Das, Cancer and Stem Cell Biology

Gastric cancer (GC) is the second most common cause of global cancer mortality with an Asian predominance. Prognosis for patients with advanced GC remains poor with a median survival of 8-12 months. Genetic abnormalities play a major role in the prognosis of cancer patients and several methods have best emerged to identify these abnormalities. We have recently identified several amplified genes in GC in the RTK/RAS signaling pathway by high-resolution single nucleotide polymorphism arrays, integrated with gene expression information and validated by fluorescence in situ hybridization (FISH). FISH is generally considered as a gold standard approach to identify individual patients who might benefit from tailored therapeutics and is widely employed in breast cancer, leukemia and more recently lung cancer. Standard FISH identifies single targets in a single sample. We now propose to develop interphase multiplex-FISH to evaluate multiple molecular targets (Her2/neu, K-RAS and FGFR2) on gastric FFPE tissues as well as circulating tumour cells (CTCs) isolated from blood of GC patients. This approach will allow identification of aneuploidies in a single slide as a one-step diagnostic procedure for cancer patients, typically giving them 3 in 1 FISH test results. The results may then be used to select the patients for different clinical trials involving the molecular targeting agents that will not only help us to move a step forward towards molecular diagnostics but also help us to accomplish a bench-to-bedside translation of knowledge.

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### 2. Domains of health-related quality of life important and relevant to cancer palliative care patients in Singapore: A preparatory study for the development of an item bank

Cheung Yin Bun, Centre for Quantitative Medicine

The measurement of quality of life of patients is embedded in the World Health Organization's definition of palliative care. It is needed for public accountability, quality improvement and research on effectiveness of care. A recent review of the literature concluded that most existing health-related quality of life (HRQoL) measures for use in palliative care patients have not been adequately evaluated. Furthermore, studies have repeatedly emphasized the importance of culture appropriateness in HRQoL assessment.

This study aims to develop culturally appropriate domain framework for measuring the HRQoL of



palliative care cancer patients, and to examine if there are content gaps in existing palliative care HRQoL measures, e.g. QAL-E, and the Patient-Reported Outcomes Measurement Information System for assessment of cancer palliative care patients in Singapore.

We will use the focus group approach to identify and define the domain framework and its elements. We will conduct focus groups with day care patients, home care patients, and outpatients with advanced cancers. Participants will be facilitated to discuss the domains of HRQoL they considered important and relevant. We will use individual in-depth interviews to supplement the focus groups.

The results of this study will form the basis for developing item banks for assessing HRQoL in palliative care patients in Singapore. The availability of HRQoL item banks for assessing palliative care recipients will represent a paradigm shift in clinical practice in Singapore. The proposed research will improve the assessment aspect of palliative care and enhance palliative care delivery and cost-effectiveness studies in Singapore.

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### **3. A critical role for mast cell responses in pathophysiology of the dengue infections**

#### 1. Soman Abraham, [Emerging Infectious Diseases](#)

The goal of the Merlion award is to fund exchange visits between research laboratories in Singapore and France to facilitate sharing of technology and the initiation of collaborative research. As a result of the award, the two laboratories plan to collaborate to examine the molecular and cellular aspects of the interactions between Dengue viruses and human mast cells, a project that builds on the findings of Dr. Ashley St. John in the Abraham Lab, which identified mast cells to be key innate immune cells that respond to dengue virus infection. The French team, including Dr. Arock and Dr. Rosine Saleh from his lab, will provide their expertise in human mast cells and will bring to Duke-NUS unique tools and reagents they have developed to allow further collaborative study of immunity to dengue virus and dengue-induced immune pathology. The funding will provide for multiple exchange visits for Drs. Abraham and Arock and their co-investigators Drs. St. John and Saleh between the two groups in Singapore and Paris, France in order to facilitate this collaboration. It is expected that valuable new information regarding the role of mast cells during human dengue infection will be obtained from these interactions and at the same time, it is anticipated that strong links between the two individual laboratories and parent institutions will be forged, which is the ultimate goal of the Merlion program.

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### **4. Characterization of induced-pluripotent stem cell-derived cardiomyocytes from patients with arrhythmogenic right ventricular cardiomyopathy for potential use as a diagnostic test**

Reginald Liew, [Cardiovascular & Metabolic Disorders](#)

#### Background:

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited heart muscle disease that is associated with life-threatening heart rhythm abnormalities and a high risk of sudden cardiac death (SCD). It is currently difficult to diagnose the condition, which can be easily missed in the early stages. Recent advances in stem cell-based technology have allowed the development of patient-specific induced pluripotent stem (iPS) cells which can be used as a powerful tool to study disease.

#### Specific aims:

In this proposal, we plan to use iPS cell technology to study the disease in more detail and

investigate whether the use of specific tests on iPS cells derived from patients with ARVC can be used as a novel diagnostic test. We aim to produce functional, living heart cells (cardiomyocytes) from patients with ARVC and other inherited heart muscle diseases to study the underlying abnormalities.

#### Research approach:

We will obtain skin samples from 18 patients (6 with ARVC) diagnosed with inherited heart muscle diseases and produce iPS cells specific to the patient. These cells will then be re-programmed into functional heart cells using techniques we have developed in our lab. We plan to study the functional and electrical properties of these heart cells using molecular biology techniques and compare these parameters with those of iPS cells obtained from skin samples from normal healthy individuals (control group).

#### Significance of research/importance to medicine

Our novel approach to studying this disease, which has never been described before, may allow for the development of a new diagnostic test for ARVC and further our understanding of the mechanisms that lead to SCD. The clinical significance of a novel test of this kind is to allow for a more patient-specific approach to diagnosis and potentially earlier detection of disease.

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## **5. Investigation on sensitivity and specificity among protein biomarkers of acute decompensated heart failure and in comparison with biomarker protein profile**

David Sim, [Cardiovascular & Metabolic Disorders](#)

#### Background:

Heart failure is a major and growing public health problem. It results not only from cardiac overload or injury but also from complex pathological conditions including genetic, neurohormonal, inflammatory, and biochemical changes acting on cardiac cells. Several studies have reported that many protein biomarkers can be used in the diagnosis and management of heart failure. However, discrepancies arise from sensitivity and specificity of individual biomarker. For instance, low level of B-type natriuretic peptide (BNP) has a high negative predictive value. However, elevated level of BNP can result from causes other than heart failure.

Multimarker approach using eighteen plasma proteins has been applied clinically in the classification and prediction of Alzheimer's disease. However, multiimarker approach in the diagnosis of heart failure has not been examined and the sensitivity and specificity of multimarker proteins in comparison with individual biomarkers are not known.

#### Hypothesis:

We hypothesize that "biomarker protein profile which is usually comprised of 5-7 biomarkers using multimarker approach is more sensitive and specific in the diagnosis of acute decompensated heart failure compared to measurement of a single biomarker. Moreover, the sensitivity and specificity will be increased by identification and addition of novel circulating biomarkers. In extending our hypothesis, we envisage that it may be possible to predict heart failure patients at risk of future events (hospitalization and death) thus allowing earlier intervention.

#### Aims:

Our primary aims is to investigate the sensitivity and specificity of each protein biomarker in the diagnosis of acute decompensated heart failure patients with ischemic heart disease etiology compared to control subjects. Our secondary aim is to identify a "biomarker protein profile" in the diagnosis of acute decompensated heart failure using Support Vector Machine Algorithm (SVM) and compare its sensitivity and specificity within protein biomarkers of acute decompensated heart failure. Finally we aim to explore and identify novel circulating biomarkers in the diagnosis of acute decompensated heart failure and compare its sensitivity and specificity with protein

biomarkers.

Methods:

We will recruit acute decompensated heart failure patients with ischemic heart disease etiology who are hospitalized and age- and sex-matched control subjects (n-150 each) at National Heart Centre Singapore following standard inclusion and exclusion criteria. Thirty-three protein biomarkers will be examined using Milliplex Assays and ELISA. "Biomarker protein profile" will be built using SVM algorithm. Novel circulating biomarkers including CD34+ cells, endothelial progenitor cells and endothelial microparticles will be enumerated with specific antibodies using FACS Calibur flow cytometer. The sensitivity and specificity of protein biomarkers, biomarker protein profile and novel circulating biomarkers in the diagnosis of acute decompensated heart failure will be compared.

Clinical significance:

Our proposal will provide us a novel approach and a sensitive and specific method in the diagnosis of acute decompensated heart failure

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## **6. Human iPS cell-derived MSCs as an important alternative cell source for the cardiovascular cell therapy of older and sicker patients**

Wei He Ming, Cardiovascular & Metabolic Disorders

Mesenchymal stem cells (MSCs) derived from patient bone marrow and adipose tissue have demonstrated clinical benefits including post myocardial infarction cardiac repair. However, the number and quality of MSCs from older patients are compromised and thus not ideal for autologous cell therapy. On the other hand, human pluripotent stem cells (hiPSCs) are embryonic stem cell (ESC)-like and are capable of unlimited self-renewal and pluripotent differentiation to almost all type of cell lineages. We have previously generated MSCs from hiPSCs (hereby named hiPSC-MSCs). Such MSCs have shown better self-renewal potential with functional superiority over bone marrow-derived MSCs.

In a recently awarded grant titled "Human iPS Cell-Derived MSCs as an Important Alternative Cell Source for the Cardiovascular Cell Therapy of Older and Sicker Patients", we planned to test the application potential of using patient-specific hiPSC-MSCs as an alternative source of MSCs for clinical therapy to aged and sick patients. In this proposed study, the feasibility of consistent generation of highly self-renewable and functionally competent hiPSC-MSCs from several patients aged over 65 with myocardial infarction and diabetes will be thoroughly evaluated. Different lines of hiPSC-MSCs will be separately derived from the hiPSCs of different patients and characterized using bone marrow MSCs derived from the same patients as controls. The pro-angiogenic potential of hiPSC-MSCs will be assessed in vitro and in vivo. Finally, hiPSC-MSC-conditioned media will be collected and the cytokine profile (e.g. VEGF) will be obtained. The potential inter-line variation will be determined.

Patient-specific or autologous hiPSC-MSCs could benefit patients of older ages with various chronic clinical conditions. The higher self-renewal potential of hiPSC-MSCs will not only allow repeated transplantation to patients who need multiple therapies but also enable the generation of function-specific hiPSC-MSCs sub-population which may deliver better therapeutic effects.

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## 7. Evolutionary consequences of reassortment on influenza A virus

Vijaykrishna Dhanasekaran, [Emerging Infectious Diseases](#)

The composition of influenza vaccine is updated in most years due to antigenic change of influenza viruses. Large-scale influenza genomic studies suggest that antigenic change in human and swine influenza viruses are linked to reassortment. However the implications of reassortment of influenza viruses is not fully understood. We hypothesize that increased antigenic change may arise following reassortment due to (i) herd-immune selection pressure, (ii) residues are under weak selective constraint, or (iii) to compensate for fitness costs accruing elsewhere in the genome. This project proposes to study implications of reassortment of influenza A viruses through in vivo experiments in order to develop a combined model of influenza virus antigenic and genetic evolution.

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