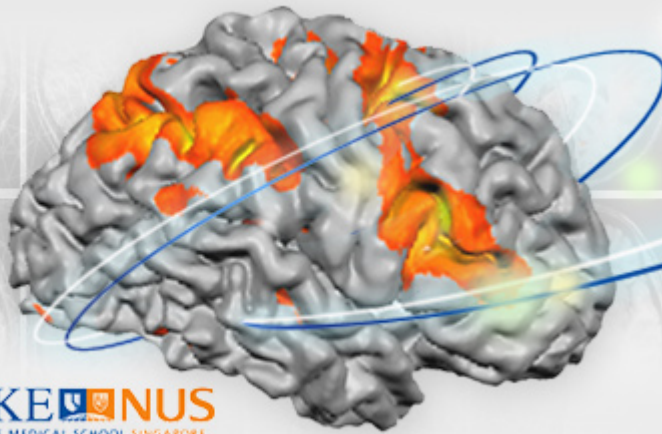


# VITAL SCIENCE

AUGUST 2009

**DUKE NUS**  
GRADUATE MEDICAL SCHOOL SINGAPORE



## Sleep Deprivation – Insights from a Cognitive Neuroscientist

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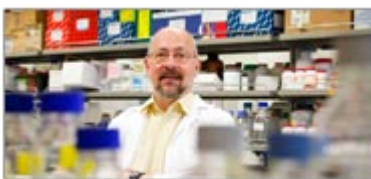
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## An Early Start to Clinical Training

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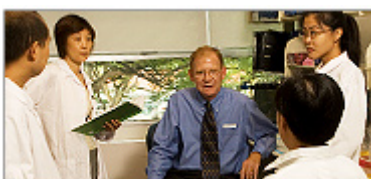
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## Brain Matters

The human brain is one giant puzzle man has devoted centuries to uncover. Understanding how the brain functions is arguably mankind's greatest intellectual challenge. Understanding the brain is also key to comprehending human biology and human behavior. Such knowledge is also essential for deducing the causes of the many neurological and psychiatric diseases stemming from impaired brain functions and for finding their cure. Dr. George Augustine is a man on a mission to understand the human brain.

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## Research Insights

In conversation with Dr. Patrick Casey, Senior Vice-Dean, Research, Duke-NUS.

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## Highlights



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## VITAL SCIENCE

Production and copy-editing: Adeline Sim

Vital Science is a quarterly publication produced by the Office of Communications and Development.

For this issue, the banner features research conducted in Dr. Michael Chee's laboratory. This image illustrates the frontal and parietal brain regions which are active when performing a working memory task.

### Duke-NUS Graduate Medical School Singapore

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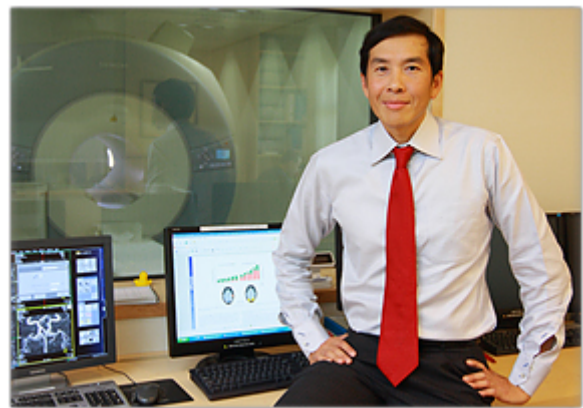
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The evolution of a doctor-scientist

Dr. Chee's career exemplifies the importance the role a doctor-scientist plays in global medicine today. Graduating as a medical doctor from NUS in 1983, Dr. Chee began his career in internal medicine, garnering broad based exposure before choosing to specialize in neurology and to sub-specialize in epilepsy and clinical neurophysiology. He trained at Tan Tock Seng Hospital in Singapore and The Cleveland Clinic in Cleveland, USA.

As his career progressed, he became more interested in Magnetic Resonance Imaging, first as a diagnostic tool and then as a means to study how the brain works. In 1996, he found himself at the intersection of engineering, neurology and psychology, and his work took a big turn: he decided to venture into cognitive neuroscience and, using fMRI, began imaging the bilingual brain.



Dr. Michael Chee is the sole recipient of the National Outstanding Clinician-Scientist Award 2009

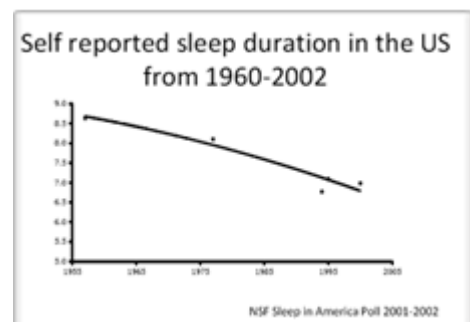
He was a special fellow at Massachusetts General Hospital's NMR Center before setting up his own lab in Singapore General Hospital and then at SingHealth. Now at Duke-NUS, Dr. Chee is a principal investigator of the Cognitive Neuroscience Lab and a member of the Neuroscience and Behavioral Disorders Program.

"I started with functional imaging in bilingualism but I wanted to get back to my roots in medicine," Dr. Chee explains. "My research now has two branches: I'm studying the underpinnings of cognitive decline as a result of sleep deprivation and I'm also interested in characterizing the aging Asian brain. I'm particularly keen in advocating for sleep deprivation of healthy adults to be used as a 'cognitive stress test' that can be potentially used to evaluate vulnerability to cognitive decline as well as its amelioration by interventions."

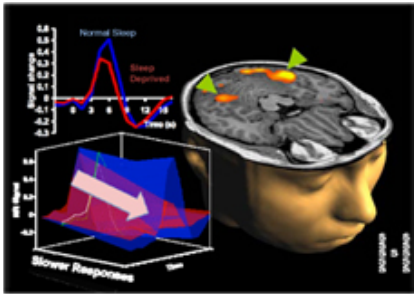
### A surge in sleep deprivation

Sleep deprivation has been shown to predispose one to obesity, high blood pressure, depression, and increase the likelihood of certain cancers. Dr. Chee takes the wider view although his focus is on cognition. "I think in modern society, especially in the age of the Internet, more and more people are spending their nights awake at work or at play," Dr. Chee says, "and they don't realize that depriving themselves of sleep with the goal of improving life may actually bring more harm than good - my focus is not on disease but in making the lives of people better."

Dr. Chee studies the effects of a night of total sleep deprivation on attention, memory, decision-making and the ability to regulate emotion. The populations most likely to benefit from his research are people whose work interferes with normal sleep patterns, such as health care workers, military personnel, professional drivers and shift workers.



“While we sleep, our memory is consolidated and possibly re-organized, repackaging what we’ve learned and experienced all day,” explains Dr. Chee. “Whether you’re an owl or a lark (a night owl or a morning person), a good night’s sleep is essential for maintaining optimal cognitive function.”



Changes in the brain signal following sleep deprivation was studied using a sustained attention paradigm. During this task, participants had to perceive and indicate the nature of the large or small letters in Navon figures (example in bottom right). Task-related brain activity declined after a night of sleep deprivation (top left graph). In addition, slow responses was associated with larger reductions in visual cortical activity in sleep-deprived individuals (brain image and bottom left graph). Adapted from Chee et al., 2008, Journal of Neuroscience. from 1960 to 2002

### **Sleep deprivation as an assay system**

In two papers, the first published in October 2008 in the Journal of Neuroscience and the second due to appear in the August 2009 issue of Sleep, Dr. Chee together with Dr. Lisa Chuah described how persons whose performance declined after being sleep deprived for a night could experience benefit from donepezil. The two studies also found that individuals who showed improvement had changes in brain activation in specifically in areas recruited to perform the different tasks. The link between behavior and brain activation changed as a function of treatment, suggesting that fMRI can be used as a means evaluate the effects of potential cognitive enhancers. The use of healthy young people as opposed to infirm elderly patients to demonstrate benefit was another key feature of these studies. “We found a reversible means to degrade cognition in young persons so that we could evaluate intervention in a safe manner.”

“Biology is such that good theory doesn’t necessarily translate to a viable treatment strategy. Some drugs that were shown to work well in animal models failed miserably in humans,” said Dr. Chee, “An important consequence of our work is that it might allow the testing of potential cognitive enhancers in relatively healthy humans, at low risk relative to trying desperate measures when one is too old.”

### **Taking the next steps**

Dr. Chee has been studying sleep deprivation for six years and given what he now knows about the system he aims to “drill into the subcomponents of attention” and on a separate track, to better understand the heritability of being able to sustain attention when sleep deprived.

“My research allows me to combine my interest in neuroscience, psychology, mathematics and technology,” he says. “Many peers aspire to own faster, bigger machines – cars, planes, watches, whatever. My dream has always been to make the best of my mind and body for as long as I can and to help others do the same. I feel privileged and fortunate that I have the tools, the opportunity and the drive to chase that dream in a country where non-tangible pursuits are often viewed with puzzlement.”

*Written by: Maureen Murray*

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## An Early Start to Clinical Training

[Click here to see slideshow >>](#)

The inaugural batch of Duke-NUS students joined hand with clinicians and healthcare professionals to make rounds in the local hospitals this year to interact with real patients and to diagnose and treat a great variety of ailments. What's unique is that the Duke-NUS students, like their Duke counterparts are only in their second year and they are seeing patients one year before their peers in other American medical school programs.

Throughout the academic year, Duke-NUS second year students go on a series of six rotations, including medicine, neurology, surgery, obstetrics and gynecology, pediatrics and psychiatry. Five one-week interdisciplinary short courses also occur throughout the year - these courses reinforce the students' understanding of the basic science behind health and disease, and also offer more in-depth understanding of the different specialties, including a section on Traditional Chinese Medicine.

Dr. Soo Khee Chee, Vice Dean for Clinical & Faculty Affairs, Duke-NUS, elaborates, "The role of our students is comparable to junior doctors and that makes them important as the rest of the clinical staff, as they contribute actively in the team to provide the best care for their patients." Dr. Soo believes that intense clinical involvement is critical in training students to be competent clinicians. "Additionally, partnering with the various teaching hospitals\* serves as an excellent and diverse learning environment for our students' clinical skills development," he adds.

Dr. Robert K. Kamei, Vice Dean of Education at Duke-NUS, agrees, "We want our students to be prepared for every possible experience in the ward. So we begin with simulated experiences as part of the training in the first year and then move the students very quickly in the wards and into the clinics and performing supervised procedures. This early, intensive, hands-on experience is a priority for our medical school."

Once on the wards, the students benefit in a myriad of ways from being a member of an actual medical team. "I call it the 'Tiger Woods factor'," Dr. Kamei says. "Watching him on TV makes golf seem so simple, but when you actually try to play it yourself, you realize it is pretty tough. When students watch a master clinician take a patient's history, examine him or her, and work with the team to come up with a diagnosis and treatment plan, it can look easy. But our students have the opportunity to actually perform these tasks themselves, to practice them and they quickly come to understand what it takes to make something look easy."





The core values of Duke-NUS are underscored in the second year curriculum: an emphasis is placed on teamwork, along with a dedication to life-long learning. The students learn and practice clinical reasoning and decision-making. They come to understand and respect the role of other health care providers on the team. And they are taught to look beyond symptoms and treatment to comprehensively care for a patient.

“We’re very proud of our students,” Dr. Kamei says. “They’re here not only to learn to practice medicine, but to change and improve the practice of medicine.”

\* Duke-NUS collaborates closely with the leading teaching hospitals and institutions in Singapore for the students’ clerkships and training. These include: Singapore General Hospital, KK Women’s & Children’s Hospital, Institute of Mental Health, National Neuroscience Institute and Changi General Hospital.

*Written by: Maureen Murray*

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## Getting an early start



Duke-NUS students Shera Chaterji and Dixon Grant get an early start on Ward 74 in Singapore General Hospital. Before 7.30am, they begin their pre-ward rounds by reading medical records and checking on elderly patients who have suffered strokes or seizures.

Typically, students starting on their clinical rotations are limited to taking histories and giving physicals, perhaps seeing each patient only once. Duke-NUS students play a bigger role in patient care. Even though they are the least experienced members of the medical team, they have more time to communicate with patients about their care and answer their questions. Because they spend more time with each patient, they complement the senior consultant's expertise by knowing more about each patient, thoroughly examining them, following up on lab work, and researching the latest information about the patient's illness. In fact, Duke-NUS students are evaluated, in part, by how much the patients see them as their doctors.

## Gaining medical knowledge



Dixon prepares for ward rounds by looking at a patient's CAT scan. "This woman had a stroke," he says. "We call it an 'evolving' stroke. The dark tissue means that tissue is dying. I'm trying to follow the evolution of the stroke because she's continuing to deteriorate and we're worried there could be bleeding in the brain later on."

The Duke-NUS medical students learn how to read scans in class during their first year, but as Dixon says, "we keep picking up more as we go along."

## Refining communications skills



*Pictured here from left: Staff nurse Tang Hui Ning; Dr. Tharma Balakrishnan, medical officer; Dr. Naomi Harun, neurology registrar; Dr. Shahul Hameed, consultant and Dixon Grant, Duke-NUS medical student.*



Dr. Hameed leads morning rounds on Ward 74, taking his team to see 10-15 patients in less than two hours. As part of Dr Hameed's team, Duke-NUS student Dixon will learn everything from taking blood performing an intake examination to obtaining a thorough personal history.

"We even learn how to introduce ourselves," Dixon explains. "Every morning I review scans of patients I haven't met yet. At first I thought communication would be easy because we're in an English-speaking country, but on this ward there's a big generation gap between the students and the neurology patients, a communications barrier that we're being taught how to overcome."

## Developing decision-making skills



*Ee Tat Xin, medical student and Brenda Lai, neuro technician at the SGH Neurophysiology Lab.*

Ee Tat Xin, a second-year Duke-NUS medical student, spends much of this rotation in SGH's Neurodiagnostic Unit, where he performs a Facial Nerve Study on a patient using electrical stimulation.

A Singaporean, Tat Xin sees the Duke-NUS medical school program as a "golden opportunity" for him. "I was very excited that this pioneer program came to Singapore. It has the best of both worlds - clinical studies and research. Initially, when I looked at the program, I felt it was so intense, almost insurmountable, but now after being here for 1 ½ years, I realize I can do it. The clinical experience is out of this world; you couldn't substitute it with books or lectures. The teaching methods here are so contemporary, truly innovative."

## Unraveling the complexities of patient care



*Duke-NUS Medical students Shera Chaterji and Pamela E-Wei Gopal with Dr. Chang Hui Meng, Senior Consultant, Neurology.*

Duke-NUS students are encouraged to approach medicine as a “systems-based” practice — where health care professionals consider the patient beyond their appointment in the clinic or stay in the hospital. The patient’s history is strongly considered as is how he or she will manage her health or illness once at home again.

At SGH’s Neurology Clinic, two Duke-NUS students spend the morning with Dr. Chang Hui Meng seeing outpatients. Dr Chang is also an adjunct Associate Professor with Duke-NUS. The first appointments of the day are for new patients who present problems such as headaches, persistent numbness, weakness and/or giddiness, a light-headed, dizzy feeling. Later in the morning, they will follow up with recently discharged patients, perhaps adjusting their medications.

## Emerging professionalism



*Pictured from left: Tushar Gosavi, registrar; Dr. Lim Shih-Hui, Senior Consultant, Neurology and Ee Tat Xin, Duke-NUS medical student*

Ee Tat Xin describes himself as being “embedded” in the Neurology team at Singapore General Hospital. Here, the team takes a break at Housemen’s Canteen. Although the conversation starts out light, the residents and students find themselves asking the consultant questions relating to medicine.

## **Relating text book learning to patients**



After morning rounds and a quick coffee break, Shera Chaterji shows slides for a presentation on delirium to consultant Dr. Lim Shih Hui, Senior Consultant, Neurology. Dr. Lim is also the Associate Professor, Education Faculty at Duke-NUS. Each of the Duke-NUS students on this rotation will give a talk on the topic of their choice to the entire Neurology department at SGH before moving on to their next assignment.

“I appreciate the opportunity to work with patients this early in my medical education. I want to help them to make a difference in their lives, to comfort them. I do my best to heal them,” says Shera.

## Catching up: In between tutorials

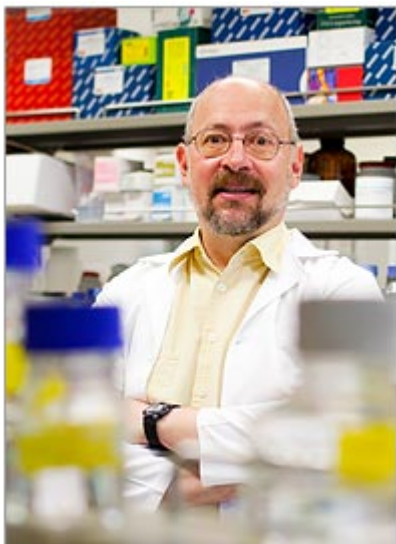


Duke-NUS students Shera Chaterji, Dixon Grant and Low Ying Hui meet up for a quick lunch before heading off to their weekly clerkship tutorial. At the end of their clerkship, they will be tested on their medical knowledge gained and also evaluated on their clinical abilities.

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*Dr. George Augustine, Neuroscience and Behavioral Disorders, Duke-NUS Graduate Medical School*

### Brain Matters

The human brain is a giant puzzle man has devoted centuries to uncovering. Understanding how the brain functions is arguably mankind's greatest intellectual challenge, and is key to comprehending human biology and human behavior. Such knowledge is also essential for deducing the causes of the many neurological and psychiatric diseases stemming from impaired brain functions and for finding their cure.

Dr. George Augustine is a man on a mission to understand the brain. His research focuses on communication between brain cells, and his team has made many contributions toward understanding the process of chemical signaling between nerve cells, and how this signaling is altered in different phases for brain activity. *Vital Science* spoke with Dr. George Augustine is a professor with the Neuroscience and Behavioral Disorders with Duke-NUS. He has highlighted some interesting facets of his favourite subject.

Dr. Augustine's laboratory is based in Biopolis, presenting ideal opportunities for research breakthrough in Duke-NUS' synergies with A\*STAR and other neuroscience partners based in Singapore.

**Editor:** **Understanding the functions of the brain is a fascinating challenge. What motivated you to do research on synaptic transmission?**

**Dr. Augustine:** When I was studying Neurophysiology at the University of New Orleans, I was exposed to the works of Dr. Katz who specialized in synaptic transmission. I like to describe Dr. Katz as the Godfather of the synaptic transmission. Dr. Katz's teaching methodologies and interpretations of synaptic transmission and principals intrigued me deeply and motivated my passion to undertake studies in this field. I believed I could get far in understanding the complexities behind the brain. Understanding synaptic transmission is the key to understanding the human brain. The brain is truly the most interesting of human organs, and this motivated me to study the complexities of brain functions. Some of the experimental symptoms on which I worked include the study of giant nerve cells in squids, which allowed me to translate the findings into the molecular biology of the brain. This aids in the understanding of synaptic transmission at the molecular level and not just on physiological observation.

**Editor:** **What is the significance of your research?**

**Dr. Augustine:** Looking at it in a more abstract way, the only thing that makes us different from very simple organisms like fruit flies is that humans have a very highly evolved brain with billions of nerve cells and synapses that allows us to think deeply and process information. A human's brain is much more sophisticated than any other living organism, as it contains more synapses that transmit more information.

**Editor:** **Which specific neurological and psychiatric diseases may benefit from your work?**



**Dr. Augustine:** Most neurological diseases and all psychological disorders are based on defects of synaptic transmission – typically arising from damage to the nerve cells. Such damage impairs the brain function because the adult brain is largely unable to regenerate or replace the damaged neurons. Some hope for ameliorating such conditions comes from recent studies showing that new neurons in fact can be generated in the adult brain. More specifically, some of these disorders that we will probably be studying include epilepsy, schizophrenia, depression, bipolar disorders and obsessive compulsive disorders.

Neurological degenerative disorders like Parkinson's and Alzheimer result from the degeneration of particular neurons in the brain. Some of our experiments will help to understand how these dying neurons can be replaced so that there is possible treatment such as transplantation therapies which involve the stem cells replacing the neurons.

Our hope is that advanced technology and research studies will help us understand these diseases better and find a way to produce a cure.



*Dr. George Augustine operating the fluorescent microscope used to image brain activity.*

**Editor:** **How has Duke-NUS impacted your research?**

**Dr. Augustine:** Optogenetics – the fusion of optics and genetics is the key factor that brought me to Singapore, and I consider this to be a revolution in research. In Singapore, we use optogenetic tools to study the wiring of the brain and we hope to work with the best scientists from around the world to study this remarkable field of research at Duke-NUS. We use molecular genetics to allow us to use one color of light to selectively stimulate certain neuron cells in the brain and another color of light to image or visualize the activity of other neurons in the brain. Thus, by stimulating one kind of neuron and seeing the responses in other neurons, it gives us insights on the wiring of the brain.

Since I joined in July 2008, it has been such a fulfilling experience for me to be part of this unique establishment that's filled with tremendous opportunities. I'm delighted and honored to work with the Duke-NUS' professors and researchers from diverse backgrounds and dynamic specializations. On average, I typically spend five months in Singapore, during which in addition to research, I conduct seminars and also give lectures on synaptic transmission related topics.

**Editor:** **What 3 things amaze you most about the brain?**

**Dr. Augustine:** **Speed** – Ask a question and you probably will get the answer in a fraction of a second. It's amazing how fast biological creation works in thought processes.

**Complexity** – A human brain contains more than 100 billion nerve cells and they form more than 100 trillion synaptic connections with other neurons. No man-made machine can compare to the brain when it comes to the richness, complexity and structure that translates back to the productive function of our senses.

**Dynamism** – Our brain is the most dynamic organ, much more sophisticated than in any other living organism. It is continuously developing remarkable feats as it absorbs new inputs.



*Research Assistant Michelle Kee and Dr. George Augustine analyzing brain imaging data.*

July 2009 - Dr. George Augustine's research program "**Adult and Induced Pluripotent Stem Cells for Neurological Disorders**", is one of the 6 research projects awarded funding under the Competitive Research Program Funding Scheme by the National Research Foundation. His team received a **\$10 million grant** to undertake this research with an ultimate objective to optimize the potential for treating degenerative neurological disorders, such as Parkinson's Disease, via cellular transplantation or by efficient deployment of endogenous neurogenesis.

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## Research Insights

In conversation with Dr. Patrick Casey, Senior Vice-Dean, Research, Duke-NUS.

**Editor:** **What is the significance of Duke-NUS as a research organization in Singapore?**

**Dr. Casey:** Nearly a decade ago Duke University embarked on the path to become an active participant in the globalization of biomedical sciences. In many ways Duke-NUS is the flagship venture of this initiative. The leadership of Duke—from former Chancellor Ralph Snyderman and Dean Sandy Williams, to current Chancellor Victor Dzau and Dean Nancy Andrews - strongly believes in the value of exposing Duke researchers and trainees to a greater diversity of cultures and practices in the biomedical arena, so that both in Durham and in Singapore our researchers have a special understanding of globalization trends and of the opportunities they present.

**Editor:** **How were the signature research programs at Duke-NUS picked?\***

**Dr. Casey:**

The research components of the Signature Research Programs (SRPs) of Duke-NUS were selected in close consultation between Duke leadership and investigators, and representatives of the Singapore stakeholders. Key considerations were:

- (i) *Competitive advantage for undertaking the research in Singapore,*
- (ii) *Potential for a substantive impact on medical needs in Singapore and southeast Asia,*  
*and*
- (iii) *Capitalization of Duke University strengths.*

We see great opportunity and potential in linking efforts at Duke with those in Singapore, and in developing our own innovative programs that leverage on applying successful strategies from Duke to diseases of regional concern.

**Editor:** **How can you translate what you do into benefits for the community?**

**Dr. Casey:**

Singapore is now well into the second phase of its Biomedical Sciences Initiative. A major component of this second phase is to strengthen translational and clinical research, and accelerate the pace at which biomedical discoveries transit into the development of products and services that can enhance the quality of healthcare for the population.

We feel that Duke-NUS is ideally positioned to play a major role in these translational medicine efforts with the successful establishment of our SRPs, together with the clinical research programs being initiated by Dr. John Rush, Vice Dean of Clinical Sciences, in collaboration with SingHealth. We aim to recruit established investigators, and develop new investigators, who will spearhead efforts to develop new treatments for diseases and better methods of delivering healthcare.

*\* The 5 Duke-NUS SRPS are: Cancer and Stem Cell Biology, Cardiovascular and Metabolic Disorders, Emerging Infectious Diseases, Health Services Research and Neuroscience and Behavioral Disorders.*

## Duke Scientists Identify Host Factors Critical to Dengue Virus Infection



Mariano Garcia-Blanco, M.D., Ph.D.  
Duke University Medical Center

Painstakingly silencing genes one at a time, scientists at Duke University Medical Center have identified dozens of proteins the dengue fever virus depends upon to grow and spread among mosquitoes and humans. Mariano Garcia-Blanco, M.D., Ph.D., professor of the emerging infectious diseases programme at Duke-NUS and professor of molecular genetics and microbiology at Duke University Medical Center, is senior author of the study.

“Dengue is a nasty disease, and currently there are no treatments or ways to prevent it,” says Garcia-Blanco, adding, “But if we can find a weakness in the virus, we can design a strategy to fight it. This study has helped us identify some gaps in dengue’s armor.”

Scientists say the study reflects the value of the growing research partnership between Duke-NUS in Singapore and Duke University Medical Center. Since opening its doors to its first class of medical students in 2007, Duke-NUS has attracted some of the top students and scientists from around the world. Garcia-Blanco says Singapore’s critical mass of knowledge about dengue was key to the success of the current study.

[View video <<](#)

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## Camp Simba

A group of Duke-NUS students organized Camp Simba, a two-day camp specially for children of cancer patients, in their first collaboration with the students from NUS Yong Loo Lin School of Medicine. The Camp, held at Costa Sands Resort, Sentosa on 30 and 31 May 2009, hosted 26 children, aged 7 to 15. The Camp was organized with the objective of providing a safe, supportive and exciting overnight experience for the children. The activities at the Camp included interactive games, trust building exercises, nature trails, art therapy sessions and tantalizing meals.



*A facilitator sharing a light-hearted moment with her camper.*



*Campers and their facilitators play a beach game.*



*The camp mascot playing with a camper.*

Dr. Ranga Krishnan, Dean, Duke-NUS and Dr. John Wong, Dean, Yong Loo Lin SOM, presented team prizes as well as awards to special helpers at an informal closing ceremony at end of the Camp. Specially commended were volunteer helpers like Pearlina Chew, Ng Guat Ngoo and Niki Goh, the nurses and psychotherapist who stayed overnight to look after the campers.

The Camp received positive feedback, as many children forged deep friendships and gained support from peers facing similar situations throughout the camp. The first reunion session after the camp was held recently on 20 June 2009 at HCA Hospice Care. The campers met up again with their facilitators and their new friends and watched a movie in the auditorium. Another two reunions have been planned for this year, one during the September school holidays and another during the December break.

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## East Meets West: Singapore-Duke Research Collaborations

Founding Dean R. Sanders Williams and Dean Ranga Krishnan collaborated to convene East Meets West: Singapore-Duke Research Collaborations, a day-long symposium held in the Levine Science Research Center in North Carolina, US, in May. The symposium featured the research synergies between Duke-NUS Graduate Medical School and Duke University School of Medicine that are bridging the faculty in Singapore and in 9,864 miles away in Durham.

Aspects in the spotlight included the global outreach of the faculty, efficiency in Singapore and support from its scientific establishment. However the key highlights were the presentations about the research programs – by at least one faculty member from both campuses. Seven program areas and the growing opportunities for Durham-based faculty to collaborate with colleagues in Singapore were covered. Among the topics of discussion were collaborations in Duke-NUS' five Signature Research Programs.



*Dr. R. Sanders Williams (left) and Dr. Ranga Krishnan (right) share notes with a colleague (centre)*



*Founding Dean R. Sanders Williams addressing faculty*

The symposium closed on a progressive note with a panel discussion where six Duke leaders shared their perspectives on the Duke-NUS partnership and its development. "This is going to change Duke," said Dr. Victor J. Dzau, Chancellor for Health Affairs, noting that together Duke and Duke-NUS are creating a vision for a 21<sup>st</sup> century global medical school.

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