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Tales from the Battlefield

Renowned researcher in new and emerging infectious diseases, Prof. Linfa Wang, shares his passion for bat-borne diseases and his vision for Duke-NUS' signature Emerging Infectious Diseases (EID) research program.

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Education Update: Making Milestones in Learning and **Teaching**

As the launch of the Academic Medicine Education Institute (AM•EI) marks another chapter in the Duke-NUS story, Professor Bob Kamei, Vice Dean of Education, and AM•El Director, shares the education milestones that are paving the way forward towards making medicine better.

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M.D. Class of 2016 gets a warm welcome

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FYI:



17 - 18 October 2012 Grand Copthorne Waterfront Hotel, Singapore



M.D. Class of 2016 View the Slideshow •



Batam Health Screening View the Slideshow ▶

VITALISCIENCE

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

Our banner story: The Academic Medicine Education Institute will give further trajectory to medical training. Read the story in "New institute for medical education launched".

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Tales from the Battlefield

Renowned researcher in new and emerging infectious diseases, Prof. Linfa Wang, shares his passion for bat-borne diseases and his vision for Duke-NUS' signature Emerging Infectious Diseases (EID) research program.

Professor Linfa Wang, Duke-NUS' new director for the EID research program and Senior Principal Research Scientist in Commonwealth Scientific and Industrial Research Organisation (CSIRO) Livestock Industries' Australian Animal Health Laboratory in Geelong, Australia, did not always aspire to be an infectious diseases expert – least of all one that specializes in bats.



Prof. Linfa Wang, Program Director, Emerging Infectious Diseases

Trained as a biochemist, the Shanghai-born Australian said, "I always say my career is determined by fate. I moved to Australia in the 1990s and saw an opening in the CSIRO for a molecular biologist. In those days, biochemists also did a bit of molecular biology, so that is where I started. I joined the CSIRO in 1990, and the first Hendra virus outbreak occurred in 1994. In 1996, we established that the virus came from bats." The rest, as they say, is history.

16 years on, Prof. Wang has won numerous scientific awards for his influential work in isolating and studying many deadly bat-borne viruses including Hendra, Nipah, and the SARS-like

coronavirus. His work has even inspired the movie, *Contagion*. "I always have to correct people, I'm not the Bat Man; I'm the Bat Virus Man," Prof. Wang points out in jest, "Everyone thinks it was visionary of me to choose to work with bats, but actually the bats chose me."

For Prof. Wang, joining the EID team has been a strategic move. For one, his experience in dealing with unknown animal viruses complements the five-year-old program's existing research strengths in dengue and influenza. "When Duke-NUS approached me for the role, I was interested. Singapore, from the emerging infectious diseases standpoint, is a hub of disease transmission. For anyone working in infectious diseases, we want to work close to the battlefield so to speak, so Singapore is an excellent place to be to do this." Prof. Wang was also impressed by the collaboration of both Duke University and NUS.

Another reason was the chance to form strategic ties between the CSIRO and Duke-NUS and tap on mutual strengths. "The CSIRO in Geelong has the world's largest bio-containment facility and expertise in animal and wildlife viruses. But Australia is geographically remote and relatively isolated with a lower risk of emerging infectious diseases. In Singapore however, we have access to a dense human population and are closer to many tropical animal-borne diseases," he explained. Working in both institutions, he said, would more "powerfully equip" him to take a holistic "one health" approach to animal and human health. After all, he pointed out, "75 per cent of emerging human infectious diseases are caused by animal-borne viruses. I can close the gap between two approaches and also bridge the expertise between Australia and Singapore."

His vision for the EID program is two-fold: to drive translational research in emerging infectious

diseases and work with stakeholders to improve Singapore's ability to respond to future outbreaks. On the research front, Prof. Wang noted how the EID program has made significant progress and "more can be done to understand why viruses cause the harm that they do."

Prof. Wang has also made it a personal commitment to meet with various government bodies and research agencies even before he took the job. "We need all the stakeholders to work together to improve the response. The EID program can play a role in providing the information on which to develop policies and response plans."

EID Research Highlights

Human antibody able to kill dengue virus discovered

A team of research scientists from Duke-NUS and the NUS Yong Loo Lin School of Medicine (YLLSoM) has discovered a human antibody that can neutralize and kill the dengue virus within two hours and found a way to reproduce this antibody in large quantities.

Principal Investigator, Associate Professor
Paul Macary from the NUS YLLSoM's
Department of Microbiology said, "This
represents the best candidate therapy that
currently exists for dengue and thus is likely
to be the first step in treating dengue-infected
patients who currently have no specific

The EID team discusses Dr. Lok Shee-Mei's team recent discovery of the dengue virus antibody. (L-R): Dr. Petra Kukkaro, Dr. Lok Shee-Mei, Dr. Ooi Eng Eong and Dr. Linfa Wang.

medicine or antibiotic to take and may take days to fully recover."

Duke-NUS' Assistant Professor Lok Shee-Mei, who was part of the team, explained that the newly discovered antibody attacks one strain of the dengue virus, DENV1, which accounts for up to half of the dengue cases in Singapore. "Our next quest is to find other antibodies that treat Dengue serotypes 2, 3 and 4 infections. We hope to combine these antibodies into one concoction in the near future."

Antiviral for dengue fever on trial

SGH and Duke-NUS have started Singapore's first trial of an antiviral medicine for the treatment of dengue fever. The antiviral medicine called Celgosivir is derived from a natural compound found in the seeds of the Moreton Bay Chestnut tree.

Associate Professor Subhash Vasudevan, who directs the Emerging Infectious Diseases Therapeutics Laboratory at Duke-NUS, explained that the clinical trial will investigate whether Celgosivir can be used as a potential treatment for dengue fever by lowering the amount of virus in the blood and



The Celaden team (L-R): Dr. Cynthia Sung, Sister Catherine Chua, Dr. Jenny Low, Dr. Subhash Vasudevan and Dr. Ooi Eng Eong.

reducing the painful symptoms and fever. "Laboratory experiments at Duke-NUS have shown that Celgosivir inhibits all four serotypes of dengue virus and improves survival in infected mice so we are taking this important next step to find out how well it works in patients," he said

Those who suspect they are suffering from dengue fever and have had fever for only a day or

so may visit their doctors at polyclinics and GP clinics around Singapore for a simple blood test to confirm the diagnosis. Patients identified with early stages of dengue fever may be referred to the CELgosivir as a treatment Against DENgue (CELADEN) trial at the Investigational Medicine Unit (IMU) located at SGH. They will receive either Celgosivir or a placebo, stay for five days in the treatment suites at the IMU and return for three visits after discharge. The medicine and treatment will be free.

The trial is carried out under the STOP Dengue Translational Clinical Research Program. Visit www.celaden.sg for details.

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As the launch of the Academic Medicine Education Institute (AM•EI) marks another chapter in the Duke-NUS story, Professor Bob Kamei, Vice Dean of Education, and AM•El Director, shares the education milestones that are paving the way forward towards making medicine better.

Teaching others to teach better: that's the premise of the AM•EI, the first such institution in Singapore. According to Prof. Bob Kamei, it will be a platform for teachers to develop areas of expertise in medical education. "The AM•EI is an opportunity for Duke-NUS and SingHealth to take an academic approach to education and look to how we can constantly improve our pedagogic methods. We see it as Singapore's National Institute of Education of medical education."



shared Prof. Kamei. "It will be a national resource, Prof. Bob Kamei a place for expert educators to come together to

share specialized expertise across the spectrum of healthcare, from medical science, nursing, allied healthcare and so on." He emphasized that teaching doctors to teach better is a critical skill. "The transfer of knowledge is essential to improve patient care," he noted, "What the AM•EI does is bridge the gap between research knowledge and patient care so doctors and healthcare professionals can take new knowledge and teach it for others to use in the way they care for patients."

TeamLEAD Report Card



TeamLEAD in action: Students learn from each other as they exchange ideas to solve the problems.

Team-based learning has been an intriguing concept in education that focuses on peer teaching, collaboration and self-directed learning. While the concept has been around for about 40 years, it has never been applied full-scale in an academic curriculum – least of all the medical sciences. But putting this theory into practice has been a distinctive move for Duke-NUS, noted Prof. Kamei – and it has paid off.

"Traditionally, Medicine has been taught in big lecture halls and with a lot of memory work. But we have adapted team-based learning concepts

for our field, reshaped it to suit our needs and called it TeamLEAD (Learn, Engage, Apply, Develop). Furthermore we have included numerous IT-based innovations, such as voiceannotated presentations where we put voice to slides."

"The fact that our students not only learn better than their US counterparts – as reflected in test scores - but do it in half the time, has validated the success of our approach and belief that team-based learning can be done on a wide scale in a medical school," added Prof. Kamei. These findings and more were published in a paper, "21st Century Learning in Medicine: Traditional Teaching versus Team-based Learning", in the Medical Science Educator in June

2012.

"What's significant is that we show how we have managed to apply our unique model of team-based learning in the entire basic sciences curriculum as opposed to previously where the concept has only been used in one or two courses. We have shown that the theory works for medical education and our students learn well using this method. However the real effect that we hope to elucidate in the long term is that our doctors will be better equipped to work in teams, which is what modern medicine is about," he explained.

TeamLEAD Fellowship program

156 delegates from 27 countries have visited Duke-NUS over the past five years to observe the TeamLEAD process. Study visits aside, said Prof. Kamei, "We were getting increasing requests from various groups to help them implement the idea. We decided to approach this idea in a more sustained – rather than ad hoc – way and designed a fellowship program to help teach others about the approach." The TeamLEAD fellowship is a 1.5-year program that includes



three visits and on-going support from Duke-NUS," *The Brunei delegation with Prof. Bob Kamei (in white* explained Prof. Kamei, "This is to help participants *shirt) on one of their TeamLEAD visits.* engage in the TeamLEAD process, design their

own approach, test it and tweak it to shape it for their specific needs." Already, the fellowship has attracted 26 participants from countries such as Japan, Brunei, Philippines, Tanzania and Saudi Arabia.

Aid for Cambodia: Elevating medical education

Significantly, Cambodia too has signed on to the TeamLEAD fellowship scheme, aided in part by a United States Agency for International Development (USAID) grant awarded to Duke-NUS. "We hope that through the TeamLEAD fellowship, we can address the brain drain of medical expertise by enhancing educational efforts to elevate the level of medical learning and continuing education for Cambodian doctors," said Prof. Kamei. To this end, Duke-NUS aims to help develop a Clinical Skills Teaching Center to provide the curriculum, materials and faculty, staff and student training for pre-clinical clinical skills training and clinical program; advise the University of Health and Sciences, Cambodia regarding the resources needed to accomplish the learning objectives at each year of schooling; provide assistance and support in developing and sustaining the program and evaluating the impact of the program. TeamLEAD-based facilitator training workshops have already been rolled out to some 20 participants in Phnom Penh.

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The Class of 2016 was warmly welcomed into the Duke-NUS family with introductory talks, team-building activities and foundational workshops that imparted skills and knowledge on how to set the right foundations, bond with peers, work with mentors and understand the school's vision and culture.

The busy but exciting foundations course, held from July 25 to August 17, also comprised ice-breaking and team-building games, an 'Amazing Race' and a barbeque hosted by senior students. Talks and introductions by senior staff and management were also held to share the Duke-NUS education approach, while senior students hosted sharing sessions on student life. The new class also took a tour of the facilities and classrooms.

What distinguished the orientation was a two-day Corporate Education (CE) workshop. Where most medical students begin their courses with science basics such as anatomy, physiology and cell biology, Duke-NUS first year students all start with a taste of team-building, negotiation skills, conflict resolution and leadership. Instructor, Nikhil Raval, Managing Director, Duke CE (India), explained: "The workshop has a blend of theory and practice. What makes it more memorable and fun for students is they get to apply the various concepts and frameworks of a well-functioning team through role-plays and simulations to deal with conflict, feedback, diversity and cultural differences."

Under the program, students also learn how to develop an action plan of shared purpose and vision for teams, undergo personality profiling, find out how to communicate effectively, and learn from other experiences and case studies.

The premise is to impart useful skills that will help them work in multidisciplinary care teams. As John Malitoris, Executive Director, Duke CE, points out, "As medicine and the profession evolve, collaboration and creativity become increasingly important in individual and overall success. Duke CE's work during the Foundations Program is structured to help the new student teams appreciate the value they can create together and organize to take best advantage of their capabilities. By getting a strong start – and Nikhil and I coming back in the Fall to check in with the teams - we hope to establish a pattern of creative success that stays with the individuals throughout the program and into their career." The Duke CE program is a leader in its field, having topped the Financial Times' Business Education Ranks for the past decade.

Ho Shu Fang, who has an accounting background, is among Duke-NUS' fresh new faces. A tipping point that spurred her decision to switch to medicine from a career in the financial industry, came after her tsunami relief efforts in Japan last year. "I asked myself, if a disaster were to happen in Singapore, what can I do for my country? I could only come up with one answer: 'I could drive people to the shelters' ... This self-reflection made me re-examine my life, the significance of my achievements and what I want to do with the rest of my life," she said. Medicine was the answer and Duke-NUS was the school of choice. "I was drawn to Duke-NUS because I was looking for a



Year 1 students out on their "Amazing Race".

school that could teach me well. I like the idea that Duke-NUS engages practising clinicians from SGH to mentor students and adopts cutting-edge learning techniques to impart the intense medical knowledge and clinical skills. Most importantly, more than half of the four years that I am spending here will be in clinical wards interacting with patients. That is where I feel most learning will take place."



Ho Shu Fang & Koh Yiwen share their aspirations as doctors-to-be.

For Koh Yiwen who is trained in nursing, she was led to take up Medicine to push her personal limits. "While nursing is an immensely meaningful and rewarding career, I felt that the role of a doctor is a more intellectually challenging and an autonomous one. To cite an analogy, instead of being the nurse who is trained to instinctively raise the patient's oxygen supply when he appears to be increasingly breathless in the hospital unit, I want to be the doctor who is able to consider all the differential diagnoses of acute breathlessness or desaturation and be in the position to decide what needs to be done for the patient. Therefore, it really is a personal aspiration to pursue medicine." She hopes to gain a more holistic understanding of the complex interaction between disease and patients. Apart from being attracted to Duke-NUS' academic rigor and research focus, as well as the increased time spent with patients, she chose the school because she was drawn to its culture. "The students, faculty members and staff in Duke-NUS are such incredibly supportive and enthusiastic people. I know studying here will definitely be a blast!"

Related story:

Welcoming our sixth class

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New institute for medical education launched

To coincide with Teachers' Day, the Academic Medicine Education Institute (AM•EI) was officially launched on September 6, 2012 at Duke-NUS. The institute is another important milestone in Duke-NUS and SingHealth's education partnership to enhance the learning environment for our educators and students. The lunch-time event attracted over 250 invited guests and doctors, nurses and allied health professionals, who came to show their avid support.







Having fun at the AM•El photo booth.

Dean Ranga Krishnan, Duke-NUS and Prof. Ivy Ng, SingHealth Group CEO gave the welcome address before the AM•EI was officially launched by the four Golden Apple Awards winners: Mr. Ow Yong Lai Meng, Principal Medical Social Worker, Department of Medical Social Services, Singapore General Hospital, Assoc. Prof. Darren Koh, Senior Consultant, Department of Anesthesiology, Singapore General Hospital, Ms. Chua Lee Kheng, Nurse Educator, Nursing Development Unit, National Heart Center Singapore and Dr. Tin Aung Soe, Analyst, Center for Health Services Research, Singapore Health Services. They each represented the medical, nursing, allied health and research professions. Holding on to 'A-M-E-I' respectively, the AM•EI was launched as they pieced the four letters together, in a show of synergy and unity.



The AM•El is officially launched.



Nurses commemorating 'Teachers' Day'

A collaboration between SingHealth and Duke-NUS, the AM•EI aims to create a vibrant community of clinician educators. Open to all in the healthcare profession, the AM•EI brings together educators and leaders to foster excellence in teaching and learning, to promote medical education research. The aim is to build a pool of educators who are passionate in developing and nurturing the next generation of healthcare professionals towards excellence in patient care.

Legacy for medical education

The newly-established Academic Medicine Education Institute (AM•EI) is grateful to receive its first major donation from the late Mr. Tan Yew Hock. His endowed gift of S\$1,000,000 will help fund faculty development programs to train healthcare educators.

Mr. Tan worked in Singapore Airlines his whole life and was known to the people around him as a hardworking and considerate man. He did not live a lavish lifestyle and through judicious personal investments, accumulated the funds that would later help many patients. His battle with cancer, coupled with the diligent care from Dr. Koo Wen Hsin, National Cancer Center staff and Singapore General Hospital Ward 78 staff, convinced him that donating to a medically-related initiative was a worthwhile cause.

As in life, Mr. Tan wanted to support something that would grow a legacy. It was with this in mind that he decided to set up an endowed fund, so that his donation can continue to benefit generations after him. We thank the estate and family of the late Mr. Tan Yew Hock for the generous gift to the AM•EI which would help fund faculty development programs to nurture and cultivate many generations of medical educators. His legacy will be a great inspiration to many medical students,



The late Mr. Tan Yew Hock

practitioners and their patients. The funds donated to AM•EI will ultimately improve the quality of healthcare in the region.

If you would like to find out more about how Academic Medicine can improve patient outcomes or would like to make a contribution, please contact the Duke-NUS Development team at 6516 2585. For more information about Academic Medicine, log on to www.duke-nus.edu.sg/academic-medicine

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Welcoming our sixth class

The M.D. Class of 2016 was officially welcomed into the portals of Medicine on Friday, August 17, during Duke-NUS' 6th White Coat Ceremony. Guest-of-Honor Ms. Chan Lai Fung, Permanent Secretary (Education Policy), Ministry of Education, Mr. Tony Chew, Duke-NUS Board Chairman as well as members of the Duke-NUS Governing Board, graced the event at the College of Medicine Building Auditorium.



The M.D. Class of 2016 with Guest-of-Honor, PS Ms. Chan Lai Fung (front center) and Duke-NUS leaders.

As the new class of students proudly donned their white coats and recited the Hippocratic Oath administered by Dr. Robert Kamei, Vice Dean (Education), they dedicated themselves to upholding the core values of Medicine.

In his welcome address to the class, Dean Ranga Krishnan said that, "there is an art to medicine as well as science," and that as doctors in training, they are expected "to serve patients responsibly and ethically and to treat them with humility, grace, and dignity." Dean Krishnan added that while there are high expectations of the class as it is "standing on the shoulders of all medical graduates, the leaders of medicine and the scientists from Duke and NUS," he advised the students to "make time for those you love and for yourself," despite their busy schedules.







(L-R): Geraldine Leow, Jasmine Goh, Lee Man Xin and Chong Xiao Yun share their joy.

After the ceremony, the Class of 2016 gathered together with key faculty members for a customary group photo, which was followed by a dinner reception at the Duke-NUS atrium.

Over half of Class of 2016 are Singaporeans and Singapore permanent residents; with the other students coming from India, Pakistan, Japan, USA, Canada, China and Bangladesh and other countries.

View gallery:



Bright smiles from Associate Dean Karen Chang and Dr. Robert Kamei, Vice Dean (Education) as they welcome guests to the ceremony.



Dean Ranga Krishnan gives the Welcome Address.



Guest-of-Honor Ms. Chan Lai Fung, Education Permanent Secretary, giving her speech.



Dean Ranga Krishnan presents the white coat to Wang Xiaohui.



Mr. Tony Chew, Duke-NUS Board Chairman, congratulates Alfred Wong on his entry to the medical community.



The Class of 2016 reciting the Hippocratic Oath.



Dr. Robert Kamei, Vice Dean (Education), having a chat with Kenneth Chin and his parents.



The Class of 2016 sharing their joy with Dean Ranga Krishnan.

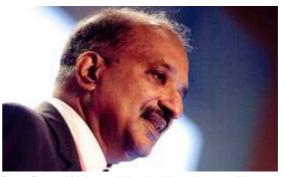
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SingHealth Duke-NUS Scientific Congress

Held in collaboration with SingHealth, the second SingHealth and Duke-NUS Scientific Congress 2012 took place in early August at the Raffles City Convention Center. The event was graced by Guest-of-Honor, Minister for Health Mr. Gan Kim Yong, and attended by more than 2,500 multidisciplinary medical, nursing, allied health and research professionals, academic scholars and overseas healthcare leaders.







Dean Ranga Krishnan delivering his welcome address.

Academic Medicine was a strong focus, with a distinctive group of healthcare professionals sharing their clinical and research findings, skills and experiences.

Professor Ivy Ng, Group Chief Executive Officer, SingHealth, voiced her confidence and support for this year's congress, pointing out that the event will "serve as an incubator for ideas and discoveries as we find more innovative ways to deliver better care to our patients."

Echoing her sentiments, Professor Ranga Krishnan, Dean of Duke-NUS Graduate Medical School, commented: "The evolving healthcare environment has created opportunities for us to leverage deeper collaborations that integrate cutting-edge clinical and translational research. This strong collaborative spirit will help boost Singapore's biomedical science landscape and strengthen the potential to develop new treatments and better outcomes that will benefit patients."

One of the congress' key highlights is the inaugural presentation of the SingHealth Academy Duke-NUS Golden Apple Awards. Recognizing outstanding SingHealth and Duke-NUS educators, the awards were presented to 12 winners from the Medical, Nursing, Allied Health and Research categories. Winners were chosen by a panel of judges made up of healthcare and education leaders and faculty members.



Research Institute.



Prof. John Rush speaking on the Academic Medicine's Prof. Sandy Cook sharing Duke-NUS' progress and the future of medical education.

The congress also received more than 500 submissions for the SingHealth Duke-NUS Scientific Congress abstract awards which recognize research excellence in basic, translational, clinical, evidence-based research and health services and systems research. Aimed at encouraging healthcare professionals to pursue ideas and innovations that improve patient care, the submissions were whittled down to 36 awards in 10 categories. The categories include 'Best Oral Presentation' and 'Best Posters' awards. 15 awards were garnered by Duke-NUS alumni, students and faculty.

Batam Health Screening

The Citramas Foundation, Duke-NUS, KK Women's and Children's Hospital (KKH) and the Indonesian Red Cross Society held its annual Batam health screening exercise on July 14 and 15 this year. 16 Duke-NUS students, together with eight KKH pediatricians, nurses and local Indonesian doctors screened 1,000 children within two days.

We were involved in many aspects of the screening exercise such as workflow planning, crowd control, recording the children's height and weight and running our own clinic under the senior doctors' supervision. To better tackle the health issues plaguing the children there, data was collected to help us plan our future visits. Within those two days, we saw many conditions, from chronic cases like malnutrition to the acute problem of extreme prematurity and dehydration.

We have gained many insights from this project which have validated our belief in the value of community service. We are indeed looking forward to the next project!

- Contributed by Galih Kunarso, MS4, Class of 2013

View gallery:



Martin and Vincent carrying out equipment checks before the screening commenced.



Words of wisdom: senior doctors providing guidance to our students.



To ensure an orderly flow, our students guided the parents to the various stations.



Our students tending to the children with the help of the local medical personnel.



The local medical personnel packing food supplies for the children.



The health screening in progress.



Martin's valiant attempts failed to get the baby's attention!



Our students earnestly and diligently carrying out the health checks.





All in a day's work: Despite the hectic weekend, the students leave satisfied with their good work and new friendships formed.

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Lien Center for Palliative Care hosts Distinguished Guests

The Lien Center for Palliative Care (LCPC) at Duke-NUS hosted Drs. J Andrew Billings and Susan Block who spoke at the Singapore Palliative Care Conference 2012, in July. They also conducted a three-day workshop on palliative care, adapted from the very successful Harvard Medical School's Program in Palliative Care Education and Practice (PCEP).



The Distinguished Guests with MOH Director of Medical Services Prof. Satku (right) and LCPC Education Director Dr. Noreen Chan.

Their week-long program included visits to local palliative care providers, giving lectures and facilitating a teaching session with Palliative Medicine Advanced Trainees. They also called upon Professor K. Satku, Director of Medical Services (MOH), and discussed various topics including palliative care for non-cancer patients, palliative care education and aspects of residency

training.



Drs. J Andrew Billings and Susan Block visited Duke-NUS.



Dr. Susan Block spoke to a capacity crowd at the HCA Hospice Care Auditorium.

- Contributed by Dr. Noreen Chan, LCPC Education Director

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New study points to the benefits of genotyping for newlydiagnosed epilepsy patients

A study undertaken by Duke-NUS researchers has found that genotyping is a cost-effective means to prevent serious adverse drug-induced reactions for newly-diagnosed epilepsy cases in the Chinese and Malay population in Singapore who carry a specific genetic variant.

The study was authored by Duke-NUS PhD student Dong Di, under the supervision of her mentor and the paper's senior author, Dr. Eric Finkelstein, Deputy Director and Associate Professor of Duke-NUS' Health Services & Systems Research Program, and Dr. Cynthia Sung, a Duke-NUS Adjunct Associate Professor and Visiting Consultant to the Health Sciences Authority.



(L-R): Dr. Cynthia Sung, Dong Di and Dr. Eric Finkelstein

The study sought to evaluate the benefits and costs to the healthcare system if all patients with newly-diagnosed epilepsy are given a genotyping test in order to avoid rare but serious and potentially life-threatening side effects. The test, which costs over S\$200, detects for the presence of the HLA-B*1502 allele. Carriers have an elevated risk of developing Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) when treated with the anti-epileptic drugs (AEDs) carbamazepine (CBZ) and phenytoin (PHT), while non-carriers have almost no risk of this condition and can be safely prescribed this effective and low-cost medicine.

"Our analysis identifies circumstances in which genotyping and targeted treatment with alternative anti-epileptic drugs that do not induce SJS/TEN is likely to be more cost-effective than treatment with CBZ or PHT without genotyping, or providing a more expensive drug that does not

induce SJS/TEN to all patients without genotyping." explained Ms. Dong.

According to senior author Dr. Finkelstein, the study is highly relevant to medical practice in Singapore, and countries in the region such as Malaysia, Thailand and the Phillipines, which have populations with a significant percentage of carriers of the HLA-B*1502 allele. The study also suggests that genotyping may not be cost-effective for populations for which the allele is rare, such as Singapore Indians, northern Chinese, Japanese and Koreans.

"This is the first comprehensive cost-effectiveness evaluation of genotyping the HLA-B*1502 allele," he said, "With the results, patients, doctors and regulatory bodies are able to weigh the costs and benefits of genotyping and decide which approach is best."

The study was published online in the journal *Neurology* on September 6.

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Methods Guide for Authors of Systematic Reviews of Medical Tests

Faced with a burgeoning number of medical tests, ranging from the conventional to the newest genetic tests and other biomarkers, clinicians and policy makers have sought insight through comprehensive reviews of the scientific literature. To help guide this process, the US Agency for Healthcare Research and Quality (AHRQ) commissioned a report, **The Methods Guide for Authors of Systematic Reviews of Medical Tests**. Produced by experienced researchers and edited by Professor David Matchar of Duke-NUS Graduate Medical School/Duke University, Durham, USA, and Dr. Stephanie Chang of AHRQ, this report provides a practical resource. Most importantly, it offers a touchstone for the challenging and potentially contentious task of assessing medical tests. The document reinforces the key principle that the value of tests must be considered in the context in which they will be used and in terms of outcomes of importance to patients and other stakeholders.

The Guide has international and local relevance since systematic reviews are often critical in clinical and policy recommendations about the use and funding of medical tests. These recommendations have often been based on studies that show a simple correlation between the test result and the presence of a particular condition or health outcome, even though the evidence may not apply in actual practice, and use of the test may not lead to better treatment decisions. The recent debates regarding the value of mammography and Prostate Specific Antigen (PSA) screening provide vivid cases in point.



Dr. David Matchar

In addition to serving as editor, Professor Matchar was author of six of the papers in the Guide. He is the director of Health Services and Systems Research (HSSR) program at Duke-NUS and is a senior faculty of Duke.

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GRANTS AWARDED

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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.	Eric Finkelstein	HSSR	A blueprint of identifying a successful walking program targeting Singaporeans age 50+	NUS Ageing Integrative Research Cluster & Virtual Institute for the Study of Ageing	12
2.	Young Kyung Do	HSSR	The labour market impact of caregiving in Singapore	NUS Ageing Integrative Research Cluster & Virtual Institute for the Study of Ageing	12
3.	Duane Gubler	EID	Development of a spatial Eco health framework to identify indicators associated with emerging infectious disease risk	NUS Initiative to Improve Health in Asia (NIHA) 2011	18

4.	Eric Finkelstein	HSSR	A Randomised Incentive-Based weight loss trial in Singapore	NUS Initiative to Improve Health in Asia (NIHA) 2011	24
5.	Scott Summers	CVMD	Isaria Sinclairii and Cordyceps Extracts for the Treatment of Insulin Resistance and Impaired Glucose Tolerance	2011 Nutrition and Food Science Grant Call	36
6.	Cheung Yin Bun	OCS	Novel statistical methods for analysis of complex clinical, serological and biological data in vaccine research	NMRC Clinical Scientist Award Nov 2011	60
7.	Lee Tih Shih	NBD	A Brain-Computer Interface Based Intervention versus Sham Intervention for the Treatment of ADHD - a Double-Blind Randomized Controlled Trial	NMRC CS-IRG November 2011	36
8.	Ong Sin Tiong	CSCB	Development of the therapeutic approaches to overcome drug resistance conferred by a novel BIM deletion polymorphism in chronic myelogenous leukemia and EGFR-mutated non-small-cell lung cancer	NMRC CS-IRG November 2011	36
9.	Steven Rozen	NBD	Identification of Drugs for Targeted Treatment of PTEN-Deficient Tumors	NMRC CS-IRG November 2011	36
10.	Alex Michael Ward	EID	Defining the function of ERI3 in DENV replication and selection of RNA aptamers that inhibit ERI3 activity	NMRC CBRG-NIG November 2011	24
11.	Cheong Jit Kong	CSCB	Modulation of Ras-induced autophagy via genetic and pharmacological targeting of a protein kinase: a novel anti-cancer strategy	NMRC CBRG-NIG November 2011	24
12.	Hsieh Po-Jang	NBD	Neural Causes of Cognitive Decision Making	NMRC CBRG-NIG November 2011	36
13.	Zhou Wei	NBD	Investigation of a Novel Stress Repressor, CReP in Human Renal Cell Carcinomas	NMRC CBRG-NIG November 2011	24
14.	David Silver	CVMD	Biochemical Mechanisms of Triglyceride Droplet Formation	NMRC CBRG November 2011	36
15.	Manoj Krishnan	EID	Role of Ubiquitin like proteins in antiviral response	MOE Tier 2 Feb 2012	36
16.	Hyunsoo Shawn Je	NBD	Regulation of BDNF exocytosis and interneuron synapse by disbindin-1	MOE Tier 2 Feb 2012	36
17.	Antonius vanDongen	NBD	Arc controls long term memory through an epigenetic mechanism	MOE Tier 2 Feb 2012	36
18.	Sun Lei	CVMD	Regulation of Brown Fat Development by Non-coding RNAs	NRF Fellowship, Class of 2012	60

19.	Young Kyung Do	HSSR	Feasibility of Using a Smart Phone Application for Self-titration of Insulin on Glycemic Control in Patients with Type 2 Diabetes	Tanoto Initiative for Diabetes Research	24
20.	Paul Yen	CVMD	Effects of 4 Month Therapy of Levothyroxine on Non-alcoholic Fatty Liver Disease (NAFLD) and Diabetes Control in Diabetic Chinese Male Patients	Tanoto Initiative for Diabetes Research	24

Total Amount of Funding Received: \$21,284,957.45

Synopsis

1. A blueprint of identifying a successful walking program targeting Singaporeans age 50+

Eric Finkelstein, Health Services & Systems Research

The goal of this proposal is to develop a physical activity program expected to have high uptake among older adults, partly through the use of modest financial incentives, in efforts to identify an effective long term strategy for increasing physical levels among older Singaporeans. The study proposes to conduct an in-home nationally representative state preference conjoint survey aimed at identifying options for low cost, scalable, physical activity programs targeting older adults, and to conduct a 3 month pilot randomized control trial (RCT) of 100 older adults (aged 50+) to test the effectiveness of a model program in Singapore.

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2. The labour market impact of caregiving in Singapore

Young Kyung Do, Health Services & Systems Research

With the rapidly aging population in Singapore, its economic impacts are receiving more policy attention than ever. While most interest has focused on the loss of labor supply due directly to the elderly leaving the labor force, some of the secondary labor supply effects, particularly those associated with caregiving, may be of comparable or greater importance. As adult children take on caregiving for their elderly parents they often must make a trade-off between caregiving and usual employment. However, little is known about how informal caregiving affects labor market outcomes in Singapore, where it is common to employ foreign domestic workers as alternative caregivers. The overall goal of this study is to estimate the labor market impact of caregiving in Singapore, accounting for joint decisionmaking regarding caregiving, employment, and hiring a foreign domestic worker.

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3. Development of a spatial Eco health framework to identify indicators associated with emerging infectious disease risk

Duane Gubler, Emerging Infectious Diseases

Emerging infectious diseases are a threat to both global health and global economies, while challenging public health policy. Southeast Asia is a predicted hotspot for the emergence and re-emergence of pathogens. Recent regional outbreaks of SARS, Nipah virus, and highly pathogenic avian influenza demonstrate the need for efficacious and targeted surveillance networks.

Our NIHA-funded project focuses on identifying indicator pathogen, host, and vector species that

traverse human-natural interfaces. These indicator groups we are sampling effectively act as a bridge between habitats, introducing their native parasitological fauna to naïve species. We will determine their distribution across Singapore and associate local ecological and environmental data.

Through collation of these data we will generate an ecological niche model to; better understand what variables influence pathogen community dynamics in the vertebrates and invertebrates of Singapore, guide surveillance efforts, predict areas of emergence events and develop recommendations for future policy.

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4. A Randomised Incentive-Based weight loss trial in Singapore

Eric Finkelstein, Health Services & Systems Research

This is a randomized controlled trial in collaboration with the Life Centre at SGH which seeks to (1) test the extent to which traditional or behavioral economic incentives, when combined with an existing evidence-based weight loss program, improve weight loss and weight loss maintenance and (2) compare the cost-effectiveness of each program.

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5. Isaria Sinclairii and Cordyceps Extracts for the Treatment of Insulin Resistance and Impaired Glucose Tolerance

Scott Summers, Cardiovascular & Metalbolic Disorders

Ceramides are toxic lipid metabolites that accumulate in individuals pre-disposed to diabetes Blocking ceramide production in rodents using a variety of experimental approaches (e.g. using the ceramide synthesis inhibitor myriocin) ameliorates features of diabetes and its cardiovascular complications. These data identify ceramide as one of the more toxic metabolites that accumulates in peripheral tissues.

Myriocin was originally isolated from an extract of the fruiting bodies of the fungus Isaria sinclairii (IS) and its parasitic host larva, but has not itself been approved for clinical trials in people. However, IS and related cordyceps species, which also contain myriocin, have been long-used in traditional Chinese medicine as a treatment for a plethora of conditions (e.g. diabetes, cancer, kidney problems, etc.), owing to their ability to induce an 'eternal youth' nostrum. When given to mice or rats, IS or cordyceps extracts improve insulin sensitivity and glucose tolerance and ameliorate hypertension. Thus, we hypothesize that IS or cordyceps extracts will prove to be an effective nutritional supplement capable of reducing tissue ceramide levels and warding off features of metabolic disease. We will test this hypothesis by completing the following aims: First, we will survey several IS and cordyceps species by mess spectroscopy to identify ones enriched in myriocin. Second, we will test the efficacy of the extract on insulin resistance and glucose tolerance in rodents seeking to identify the molecular basis for IS or cordyceps action.

This work is the first attempt to explore the therapeutic potential of manipulating ceramide levels using a commercially available reagent. In addition to providing proof-of-principle experiments aimed at determining whether controlling tissue ceramides may serve as an effective strategy, the study could identify an immediately available treatment for people susceptible to metabolic disease.

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6. Novel statistical methods for analysis of complex clinical, serological and biological data in vaccine research

Cheung Yin Bun, Office of Clinical Sciences

Singapore, along with the rest of South-East Asia, has experienced a substantial burden of infectious diseases. Research on vaccines and vaccination strategies are vital for protecting the people and their livelihood. Statistical analysis of clinical, serological and biological data is an important part of this research. Such data often suffer two problems: complex censoring (including detection limit) and data clumping at zero. Some commonly-used laboratory and statistical approaches to handle such problems give rise to bias in estimates of mean concentration, prevalence of true negative and association between exposure and response, as well as poor type I error control and power. Regulatory and academic researchers have raised their concerns and called for improvements in statistical methods.

This project aims to develop novel statistical methods that can improve the analysis of serological and biological data. The investigators propose to develop three sets of models for handling data with:

- undefined "fold increase" endpoints due to complex censoring in measurements at one or two time-points,
- clumps of zeros, and
- combination of censoring (detection limits) and clumps of zeros.

The development of these models will follow the principles of mixture models and (censored) time-to-event analysis. Advanced algorithms will be proposed for the estimation. The investigators will mathematically/theoretically assess their properties, and compare their performance versus that of existing methods by simulation. The investigators will also develop and validate computer macros for implementing these methods.

These novel methods will improve the accuracy of estimates and inference of important parameters needed for the evaluation of vaccines and vaccination strategies. The gain in statistical precision/power will also speed up the research process. Although this research is mainly motivated by vaccine and vaccination studies, the methodological problems are general. The results will benefit other medical research, such as studies of censored and/or zero-inflated medical expenditure data and chemical contaminant data.

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7. A Brain-Computer Interface Based Intervention versus Sham Intervention for the Treatment of ADHD - a Double-Blind Randomized Controlled Trial

Lee Tih Shih, Neuroscience and Behavioral Disorders

Introduction:

Attention deficit hyperactivity disorder (ADHD), a psychiatric condition commonly found in children, is characterized by over activity, the inability of a child to stay attentive and impulsivity. Although drug treatment is available, parents often decline drugs due to concerns about the side effects and costs. Therefore, we developed an electroencephalogram (EEG)-based brain computer interface (BCI) system as an alternative treatment to improve the child's ability to stay attentive. This locally developed system had been shown in previous pikot trials to have the capability to improve inattentive symptoms of ADHD children. In this trial, we aim to confirm the efficacy of this BCI-based treatment in a large, randomized controlled trial.

Aims:

We aim to ascertain that ADHD children who undergo our BCI-based programme will have greater improvements in inattentive symptoms as compared to controls.

Method:

160 children between the age of 6 and 12 years who have been diagnosed with ADHD but have declined the drug treatment option will be enrolled in this study. At random, they will be classified into either the treatment or control group. Children in the treatment group will receive 24 sessions of BCI-based therapy over a period of 8 weeks, followed by monthly 'booster' sessions over the

subsequent 3 months. The control group will receive the BCI-based therapy after the treatment group has completed their 24 sessions of therapy. Parents of all participating children will complete the ADHD Rating Scale (ADHD-RS) and other questionnaires before, during and after therapy. The children will also undergo neurocognitive testing. It is hoped that the BCI-based therapy will improve the inattentive score on the ADHD-RS as rated by clinicians who are not aware which group the children are in.

Significance:

If shown to be effective and safe, this newly-developed BCI-based therapy can serve as an alternative treatment option for ADHD patients who decline to be on medication. This may eventually be employed in conjunction with medications and psychosocial interventions.

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8. Development of the therapeutic approaches to overcome drug residtance conferred by a novel BIM deletion polymorphism in chronic myelogenous leukemia and EGFR-mutated non-small-cell lung cancer

Ong Sin Tiong, Cancer and Stem Cell Biology

One of the biggest success stories in cancer treatment is tyrosine kinase inhibitor drugs (TKIs), which work effectively against some blood cell cancers, such as chronic myelogenous leukemia (CML), as well as non-small-cell lung cancers with mutations in the epidermal growth factor receptor (EGFR), to shut down the pathways that keep these cancers flourishing. However, about 25 percent of patients do not respond to these precisely targeted therapies, and little has been known about the reason why. Recently, our team discovered a common variation in the BIM gene that occurs in ~15% of people of East Asian descent that contributes to resistance against the useful TKI drugs. These include the standard TKI drugs used to treat CML (imatinib (Gleevec), nilotinib (Tasigna), and dasatinib (Sprycel)), as well as those used to treat EGFR non-small-cell lung cancer (erlotinib (Tarceva) and gefitinib (Iressa)). Because we were also able to determine how the BIM gene variant caused TKI resistance, we have been able to devise a number of rational strategies to overcome TKI resistance conferred by the BIM gene variant. This grant will determine if the therapeutic strategies we propose will be able to overcome TKI resistance in cancer cells bearing the BIM variant. The validation of our strategies may lead to clinical trials in patients with TKI resistance with the BIM gene variant, and hopefully enable us to overcome this form of drug resistance in patients in East Asia.

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9. Identification of Drugs for Targeted Treatment of PTEN-Deficient Tumors

Steven Rozen, Neuroscience and Behavioral Disorders

Loss of the PTEN gene plays a key role in driving many human cancers. It is one of the most commonly mutated cancer genes, and expression of its protein product is frequently lost in many types of cancer. Nevertheless, there are no effective therapeutic approaches for treating such PTEN-deficient tumors. The overarching goal of this project is to identify drugs for the targeted treatment of PTEN-deficient tumors. This will be done in two stages. In the first stage, we will use a technique called "RNA interference" to discover which druggable genes are essential to the growth of cancer cells that have lost PTEN function. In the second stage, we will identify commercially-available drugs that target these genes and test if they are effective against a panel of PTEN-deficient cells from various types of cancer. Drugs identified in this study will have immediate translational potential as they are commercially available and the genes that they target are known. Therefore, the drugs identified will be attractive candidates for further development.

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10. Defining the function of ERI3 in DENV replication and selection of RNA aptamers that inhibit ERI3 activity

Alex Michael Ward, Emerging Infectious Diseases

Dengue virus (DENV) is a rapidly re-emerging infectious disease endemic to tropical areas of the world and of particular concern in Southeast Asia. There are currently no therapies to prevent or treat DENV infection. Previous attempts to develop DENV therapeutics have focused on small molecule inhibitors of viral enzymes, but another promising avenue for therapeutic targets is to identify host cell proteins required for DENV replication. Using genomic and proteomic techniques, we have identified a host cell exonuclease, ERI3, which is required for DENV replication and associates with DENV RNA. The first challenge is to determine the precise role of ERI3 in DENV replication and whether it functions as an exonuclease in DENV-infected cells. The second challenge is to develop a compound that inhibits ERI3 function during DENV replication. A novel approach to targeting host cell proteins is to utilize competitive RNAs, called aptamers, selected from a random library of RNAs for their ability to bind to a protein of interest. We will apply this method for developing an inhibitory RNA aptamer against ERI3 and test its ability to inhibit DENV replication. Furthermore, this system can be applied to other DENV host factors identified in genomic and proteomic screens.

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11. Modulation of Ras-induced autophagy via genetic and pharmacological targeting of a protein kinase: a novel anti-cancer strategy

Cheong Jit Kong, Cancer and Stem Cell Biology

Cancer is the leading cause of death in Singapore. Activating mutations in the RAS oncogene and inactivation of tumor suppressors are commonly found in 20-25% of all human tumors and approximately 90% in specific tumor types. Recent reports suggest that activation of oncogenic Ras alone can promote cancer and cell death, both of which exhibit features of autophagy. Autophagy is a primitive intracellular nutrient recycling process that enhances cell survival in response to stress cues like oncogenic Ras activation. Since it remains unknown whether one should promote or inhibit autophagy to improve the efficacy of our existing anti-cancer drugs for the treatment of Ras-driven cancers, ongoing research effort is required to fully understand how Ras-induced autophagy works. We recently found that a novel protein kinase is involved in the regulation of Ras-induced autophagy. In this study, we will investigate how oncogenic Ras regulates this kinase and determine how the latter modulates Ras-induced autophagy. Importantly, we will study whether genetic or pharmacological targeting of this kinase can be used to control Ras-induced autophagy. If successful, this study will uncover a new pathway that could be exploited to treat Ras-driven cancers and improve the outcome of combinatorial cancer therapy in humans.

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12. Neural Causes of Cognitive Decision Making

Hsieh Po-Jang, Neuroscience and Behavioral Disorders

Impaired decision-making is a common feature of many neurodegenerative diseases. Identifying the essential brain areas of decision-making will be the first step toward future medical treatments. Here we propose an approach that localizes the essential parts of the brain that are causally involved in human decision-making. We focus on the "neural causes" of decision-making by searching for neural antecedents that occur before and predict human decisions. Our approach goes beyond conventional paradigms that only look for the "neural correlates" of decision-making, and will grant us the ability to localize the candidate brain areas that are the "neural causes" of decision-making but not merely "neural correlates" or "neural consequences". Specifically, we investigate whether pre-stimulus brain states (i.e. baseline brain states right before stimulus presentation and decision-making) can affect evaluative decisions and their locations/means of exerting an influence if one exists. Our preliminary data show that evaluative decisions can be predicted by human subjects' pattern of fMRI signals across a widely distributed network of

regions in the frontal lobes before the stimuli are presented. Further examining the underlying neural basis could provide valuable information about decision-making in normal brain processing as well as how it can break in neurodegenerative diseases.

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13. Investigation of a Novel Stress Repressor, CReP in Human Renal Cell Carcinomas

Zhou Wei, Neuroscience and Behavioral Disorders

Renal cell carcinoma (RCC) is the most frequent type of kidney cancers. As they are resistant to chemotherapy and radiotherapy, there are very limited treatments available. In general, cancer cells are facing high level of stress due to their unique growth conditions and unlimited proliferation. One possibility to kill cancer cells is to boost cancer cell stress level. To this regard, inhibitors of stress repressors will be good candidates. Our preliminary results show, a cellular stress repressor is increased in human kidney cancers and overexpression of this protein promotes cancer cell proliferation. Based on these findings, we hypothesize that this stress repressor, is able to promote RCC cell proliferation and tumorigenesis. We will test this hypothesis in variety models of RCC, and try to understand how it functions. Because it is an attractive anti-cancer drug target, we foresee, this study will be provide guidance to design specific inhibitors as novel targeted tumor therapy for RCC.

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14. Biochemical Mechanisms of Triglyceride Droplet Formation

David Silver, Cardiovascular & Metabolic Disorders

The occurrence of obesity and consequently type 2 diabetes is becoming a worldwide problem and increases the risk of premature mortality. It is estimated that over 300 million individuals will be afflicted with type 2 diabetes by the year 2025. Obesity results not only in an expansion of fat tissue in the body, but an increase in the amount of fat that is stored in liver, skeletal muscle and heart. Increased amounts of fat stored in these tissues lead to problems with normal functioning of these organs and exacerbates type 2 diabetes. Currently, there is an unmet medical need to devise treatments to lower the levels of fat that is stored in the body. It is therefore important to identify ways to improve the ability of tissues in the body to safely store triglyceride and to prevent its buildup in muscle, liver and heart. The goal of this research proposal is to discover how tissues of the body store fat. The information obtained from this proposal will provide important insight into how tissues in the body store fat and is expected to lead to the discovery of new treatments for obesity and type 2 diabetes.

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15. Role of Ubiquitin like proteins in antiviral response

Manoj Krishnan, Emerging Infectious Diseases

The innate immune system is the most prominent arm of our body's defence against viruses during the early phase of infection. An effective innate response is critical for the development of adaptive response and subsequent infection clearance. The innate response initially involves the recognition of viruses by several pattern recognition receptors, that will subsequently induce the production of the most effective antiviral proteins called Type I Interferons (TI-IFNs). The TI-IFNs will induce a potent antiviral state in cells, and their expression is crucial for resisting viral infections. While TI-IFNs are essential for resisting infection, excessive interferon response is harmful for the body, and can cause autoimmune diseases. In this study, we aim to understand the fundamental molecular mechanisms regulating the "optimal" interferon response. The anticipated

results will catalyse further studies on both fundamental and translational aspects of interferon response.

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16. Regulation of BDNF exocytosis and interneuron synapse by disbindin-1

Hyunsoo Shawn Je, Neuroscience and Behavioral Disorders

Brain-derived neurotrophic factor (BDNF) is a small, secreted protein that plays a fundamental role in nervous system development and in regulating the strength of existing synapses throughout adult life. Imbalances in BDNF signaling impair several forms of neuronal plasticity and lead to a wide range of cognitive abnormalities. Unlike classical neurotransmitters, BDNF is preferentially synthesized in, and secreted from glutamatergic excitatory neurons via exocytosis. Despite the importance of BDNF release in brain development and plasticity, the cellular and molecular mechanisms regulating BDNF secretion and their role in interneuron development are largely unknown. Intriguingly, we recently found that the gene product of dysbindin-1, a leading candidate susceptibility gene for schizophrenia, regulates both the exocytosis of BDNF from excitatory neurons and GABAegic interneuron synapses formed on excitatory neurons. We aim to determine the mechanisms by which dysbindin-1 regulates BDNF exocytosis and how the interplay between BDNF and dysbindin-1 modulates the development of neural circuitry in the brain.

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17. Arc controls long term memory through an epigenetic mechanism

Antonius van Dongen, Neuroscience and Behavioral Disorders

Some of our childhood memories are retained for a lifetime. How such memories are stably stored in our brain for decades is incompletely understood. Formation of new memories involves functional changes in the connections made by the neurons that constitute our brain. Because neuronal connections remain 'plastic', these initially-formed memories are in danger of being over-written. Memory 'consolidation' selectively stabilizes some of these short-term memories to preserve them for future recall. A project funded by the MOE will explore in detail the molecular and cellular basis of the process of memory consolidation. Mice which lack a gene called Arc cannot consolidate memories: new memories fade away after a few hours. Our laboratory has shown that Arc protein resides in the nucleus of neurons, where it associates with structures that regulate gene expression. We are therefore testing the hypothesis that Arc controls long-term memory through an epigenetic mechanism, in which Arc expression mediates long-lasting alterations in neuronal gene expression programs.

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18. Regulation of Brown Fat Development by Non-coding RNAs

Sun Lei, Cardiovascular & Metabolic Disorders

The board objective of my research is to identify novel drug targets for the development of therapeutics that can be used to combat obesity. Obesity is a major source of morbidity and mortality, and its prevalence is rising in many areas of the world. However, available treatments for obesity are limited. Brown adipose tissue (BAT) is an attractive target for obesity treatment. Mammals have two principal types of fat. White adipose tissue (WAT) primarily serves to store extra energy triglycerides, while BAT is specialized to burn lipids for heat generation and energy expenditure. In humans, the activity of BAT negatively correlates with body mass index (BMI). Ablation of BAT in mice reduces energy expenditure, resulting in obesity development. Conversely, augmentation of BAT's activity and prevalence often prevents obesity. In light of the anti-obesity feature of BAT, the interest in understanding the mechanisms underlying BAT development is increasing. Although multiple protein factors have been identified as regulators for BAT

development, roles of non-coding genes in this process are unknown. Here, I propose to investigate the roles of non-coding RNAs including mircoRNAs and lincRNAs (large intergenic non-coding RNAs) in BAT development.

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19. Feasibility of Using a Smart Phone Application for Self-titration of Insulin on Glycemic Control in Patients with Type 2 Diabetes

Young Kyung Do, Health Services & Systems Research

Many patients with type 2 diabetes mellitus (T2DM) require insulin therapy after suboptimal glycemic control with oral antidiabetic agents. Initiating insulin therapy and adjusting dosage is vital in improving clinical outcomes among patients with diabetes. However, timely and appropriate dosage titration is challenging for many patients. Doctors also contend with many patients lacking the confidence to self-titrate insulin. Hence, reinforcing patients' self-empowerment is important in diabetes management.

Developing tools that facilitate dosage adjustment of insulin may have substantial benefits to glycemic control. This study aims to investigate the feasibility of using a patient-centered smart phone application for insulin self-titration to improve glycemic control in patients with T2DM, in addition to usual care. Secondary outcomes such as patient's health care utilization, treatment satisfaction, diabetes-related self-efficacy, and insulin perceptions will also be examined.

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20. Effects of 4 Month Therapy of Levothyroxine on Non-alcoholic Fatty Liver Disease (NAFLD) and Diabetes Control in Diabetic Chinese Male Patients

Paul Yen, Cardiovascular & Metabolic Disorders

Non-alcoholic fatty liver disease (NAFLD) is a silent epidemic that affects 60-80% of patients with Type II diabetes. It can progress from fatty liver to hepatitis to liver failure. Currently, there is no effective drug therapy available for NAFLD. Recently, we and others observed that thyroid hormone (TH), a key hormone that controls cell metabolism, has altered function in the livers of animal models and patients with NAFLD. While the precise cause is currently being investigated, it is likely that increasing serum TH levels to a range that does not give side effects may be beneficial to diabetic patients with NAFLD. We thus ask whether low dose thyroid hormone therapy can decrease fatty liver in diabetic patients with non-alcoholic fatty liver disease (NAFLD). In particular, we seek to know whether short-term low dose TH therapy can decrease fatty liver and improve serum sugar control in Type II diabetic patients with NAFLD.

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